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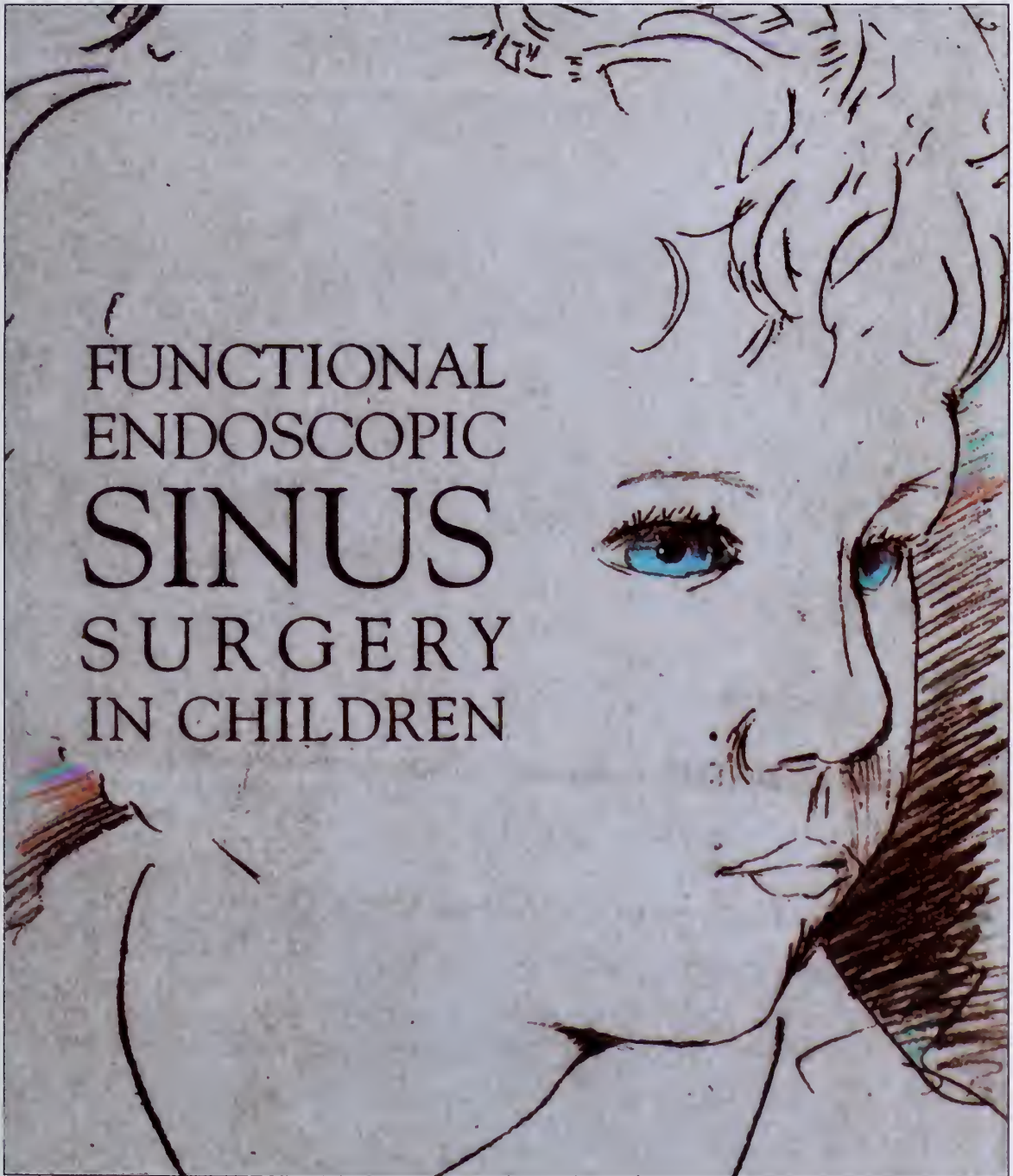
# JOURNAL

OF THE MISSISSIPPI STATE MEDICAL ASSOCIATION

JANUARY

1993

## FUNCTIONAL ENDOSCOPIC SINUS SURGERY IN CHILDREN





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OF THE MISSISSIPPI STATE MEDICAL ASSOCIATION

JANUARY 1993

VOLUME XXXIV

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## SCIENTIFIC ARTICLES

- Functional Endoscopic Sinus Surgery In Children** 1

*James R. Haltom, MD and C. Ron Cannon, MD*

- Evaluation of Mammographic Stellate Lesions** 7

*W. Mel. Flowers, Jr., MD and Cynthia I. Powers, MD*

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## SPECIAL ARTICLE

- Delegate's Report - 1992 AMA Interim Meeting of The House of Delegates** 11

## EDITORIALS

- A Tribute To Carl Evers** 14

*William C. Gates, Jr., MD*

- Medicine In 1993** 15

*Myron W. Lockey, MD*

## DEPARTMENTS

- Letters** 17

- Current Opinions** 19

- Medical Organization** 21

- From the University of Mississippi Medical Center** 25

- Personals** 28

- Placement Service** 32

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# Dateline

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## **Yearly Adolescent Check-ups May Help Reduce Health-care Costs.**

New York (AP) - An annual check-up for adolescents that includes screening for emotional and sexual problems could combat the growing health care crisis among teens and cut costs, the American Medical Association said.

The AMA recommends that annual check-ups for people ages 11-21 in its "Guidelines for Adolescent Preventive Services," which is being distributed to doctors this week. The group plans to implement the guidelines over the next several years.

Preliminary figures suggest that care would cost about \$100 per year and save about \$600 per year by avoiding health-care costs later, said Dr. Arthur Elster, director of the AMA's department of adolescent health.

An insurance company spokesman said, however, that companies were not likely to cover preventive care unless the government intervened to require all insurers to provide it.

At a news conference to release the AMA recommendations, Dr. William L. Roper, director of the federal Centers for Disease Control and Prevention in Atlanta, backed the proposal. He said traditional medical exams don't uncover the leading threats to adolescents.

For example, he said, 70 percent of deaths among people ages 1-24 are caused by car accidents, other injuries, homicide and suicide.

Twenty-six percent of high-school students say they have carried a weapon, usually a gun. Eighty-two percent have used alcohol, and 54 percent have had sexual intercourse.

"Today's young people were thrust across the threshold of a major behavioral revolution, of which changing sexual norms is only a part," Roper said.

Dr. A. Robert Davis of Nationwide Insurance Companies in Columbus, Ohio, said insurers understood the importance of prevention but for competitive reasons could not cover it.

Roper said the government must require insurers to provide coverage for preventive care. Davies agreed.

### **AMA GUIDELINES**

- All adolescents should be screened for eating disorders.
- All adolescents should be asked about tobacco, alcohol and drug use.
- Sexually active adolescents should be screened for sexually transmitted diseases.
- They should be offered confidential AIDS testing.
- All adolescents should be screened for high blood pressure and other heart-disease risks.

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## **MSMA Annual Socio-economic Forum**

MSMA's January 19, 1993 Medical Issues Forum for all MSMA members and the MSMA Auxiliary will feature national speakers on health care reform and will be followed by a reception for members of the MS Legislature. The Forum, which is co-sponsored by the MS Hospital Association, will begin with a luncheon at 12:00 noon at the Coliseum Ramada Inn in Jackson. Afternoon speakers from President-Elect Clinton's Health Care Transition Team, the Conservative Democratic Forum, the American Medical Association and the American Hospital Association will present their respective organization's views on health care reform and a Q & A session will follow. Plan to attend this important program on the nation's future health care plans. If you have not received registration material please call the MSMA office.

\*\*\*

## **125th Annual Session Scientific Exhibits**

The MSMA 125th Annual Session will be held April 28 - May 2, 1993 at the Royal d'Iberville Hotel, Biloxi. Physicians who would like to reserve **Scientific Exhibit Space** should write: **Scientific Exhibits, MSMA, PO Box 5229, Jackson, MS 39296-5229** or FAX this information to (601) 352-4834. The letter requesting exhibit space should include the following information:

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- (3) **an estimate of the amount of exhibit space needed (MSMA will provide a table - all other materials are to be supplied by the exhibitor);**  
**and**
- (4) **a brief synopsis of the subject to be exhibited.**

\*\*\*

## **MSMA Community Service Award Nominations**

Information has been sent to all Component Society presidents and secretaries soliciting nominations for the 1993 MSMA Community Service Award. The award is designed to provide recognition to members of the association, who are actively engaged in the practice of medicine, for the many and varied services above and beyond the call of duty which they render to their respective communities. The award consists of an engraved plaque and a \$500 contribution made by the association to the civic organization designated by the award recipient.

The MSMA's Council on Public Information encourages each component society to submit a nominee for this award. All nominations should be submitted by January 15, 1993 and the award will be presented during the MSMA's 125th Annual Session.

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# Functional Endoscopic Sinus Surgery In Children

JAMES R. HALTOM, MD  
C. RON CANNON, MD

**S**inus disease has long been a problematic area of pediatric medicine, particularly regarding its surgical management. Even diagnosing sinusitis in children can be difficult since their symptoms may be non-specific (nasal congestion, post-nasal drainage, malaise, malodorous breath, etc).<sup>1-5</sup> Furthermore, plain sinus x-rays lack sensitivity and can miss considerable disease.<sup>3,6</sup> Prior to the advent of accurate imaging techniques, such as the CT scan, pediatric sinus disease was often overlooked. During the last several years, however, the true extent of pediatric sinusitis has been better defined and its bacterial causes identified.<sup>3,5,7</sup> Fortunately, most children respond to appropriate medical management.<sup>8</sup> Children who do not respond to medical treatment have been an area of special concern. Previously used surgical procedures such as antral windows or the Caldwell-Luc technique have either been poorly successful or inappropriate for children.<sup>3</sup> Over the last few years,

During the last decade, the usefulness of functional endoscopic sinus surgery (FESS) has been clearly demonstrated in adult patients. Several recent studies have described the use of FESS in children. Most of the patients in these earlier studies have been school age or older. This paper will examine the follow-up of 44 children treated using FESS. The children's ages ranged from 14 months to 13 years with a mean age of 54.5 months. Thirty-three of the children were less than 6 years of age with a mean age of 35.3 months. Follow-up after surgery varied from 1 to 21 months with a mean of 7.4 months. There were no major surgical or anesthetic complications noted during the initial procedure or at the follow-up debridement. Overall the children did well, with 86% showing improvement. It appears that FESS can be helpful for even young children with chronic sinusitis.

endoscopic surgical techniques have been introduced to this country and appear to offer better hope for children with sinus disease.<sup>9-13</sup>

An illustrative case is presented. C.K., an 18 month old female had a history of persistent sinusitis exacerbating reversible obstructive airways disease and associated with several episodes of pneumonia. She had

been on antibiotics continuously for approximately 6 months prior to surgery, and her asthma was steroid dependent. Additionally, she had allergic rhinitis requiring symptomatic management.

Functional endoscopic sinus surgery was carried out including ethmoidectomies and enlargement of the natural ostia of each maxillary sinus. Within six months of her surgery, steroids



were completely discontinued, her asthma became much easier to control, and the need for antibiotics was markedly decreased.

## MATERIAL AND METHODS

During a 27 month period, 58 children under 15 years of age had functional endoscopic surgery performed. Forty-four of these children responded to a survey concerning FESS. The respondents ranged in age between 14 months and 13 years with a mean age of 54.5 months. All of these children were referred by their pediatrician or allergist due to chronic sinus disease unresponsive to aggressive medical management. Their symptoms primarily included nasal congestion, post-nasal drainage, and discolored rhinorrhea. These symptoms had been present for months despite aggressive medical management. Fourteen of the children also had moderate to severe asthma. It is noteworthy that 27 of the children attended daycare.

Each child had failed multiple courses of appropriate antibiotics plus oral decongestants. Thirty-eight of these children had received more than 10 weeks of antibiotics prior to FESS with six children receiving 5-10 weeks. Some (24 of 44) had also been treated with intranasal steroids. Thirty-one of the children had been treated for apparent allergies prior to FESS. Nineteen of these 31 (61.3%) had a history of positive prick skin tests to inhaled allergens. None of the children had known associated problems such as hypogammaglobulinemia, cystic fibrosis, or dysmotile cilia syndrome. Each child had a coronal sinus CT scan performed prior

to FESS. All of the scans showed obstruction of the ostiomeatal complexes and evidence of maxillary sinusitis. Many of the children also had involvement of their ethmoid sinuses. Seven of the children had previously un-

dergone maxillary antrostomies.

## TECHNIQUE

All of the surgeries were performed by a single surgeon (CRC) using endoscopic techniques. Visualization of the af-

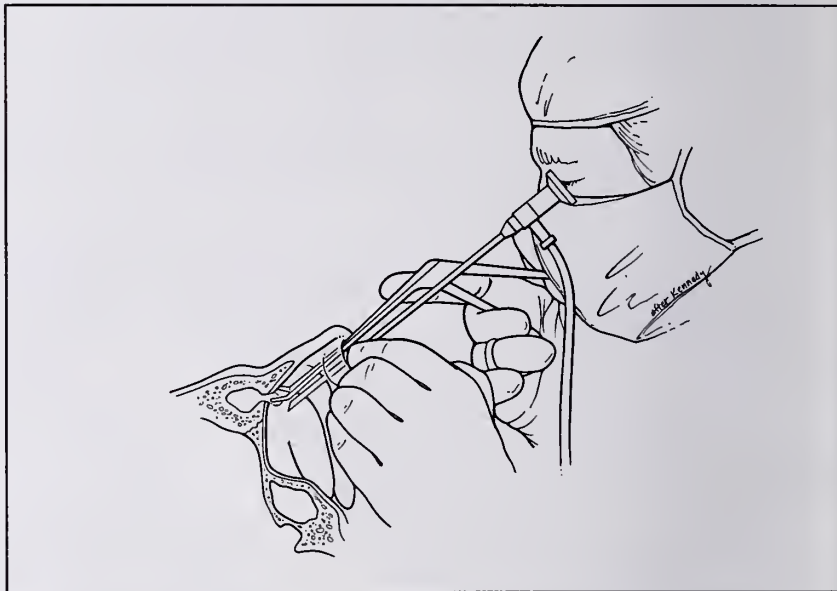


Figure 1 - Diagrammatic approach to sinuses using the endoscopic technique.



Figure 2 - Area of the ostiomeatal complex.



affected areas within the nose was achieved by use of rigid 0 degree and 30 degree telescopes (see Figure 1). A combination of special adult instruments and pediatric size instruments were used to open the affected sinuses.

The key to success for this type of surgery is an understanding that most inflammatory sinus disease arises from the anterior ethmoid and middle meatus of the nose, known as the ostiomeatal complex (see Fig-

ure 2). The purpose of FESS is to re-establish sinus ventilation and mucoallary drainage of the sinuses. Patency rates for this type of surgery have been studied previously in adults and found to >90%.<sup>9</sup> It is felt that mucocilliary clearance occurs through the surgically opened ostia of the sinuses.

Using a small sickle knife, an incision is made in the region of the ethmoid infundibulum (see Figure 3). The ethmoid sinus is

entered and hypertrophied mucosa removed. Care must be taken to avoid the orbit laterally and the cribiform plate of the skull base superiorly. As the frontal sinus is usually not developed in children, no attention to this area is needed. Occasionally the sphenoid sinus is developed and may require opening after the posterior ethmoid cells have been ablated.

The next portion of the procedure is directed at opening the ostium of the maxillary sinus. The ostia may be difficult to visualize due to inflamed mucosa. The ostia is often palpated with a curved suture tip and the slus entered. Any purulent material is sent for the appropriate culture and sensitivity studies.

The maxillary sinus ostium is then enlarged anteriorly with special back biting forceps taking care to avoid the nasolacrimal duct (see Figure 4). The nasolacrimal duct is located in the thickened bone of the medial portion of the maxillary sinus. A palpable change in the thickness of the bones serves as a limiting landmark to avoid surgical trauma in this area. The mucosa within the maxillary sinus can now be visualized and removed transnasally if it appears irreversibly damaged.

Nasal packing is generally not required. Antibiotic ointment is injected via a syringe into the operative sites.

A crucial part of the procedure is follow-up cleaning of the operative sites. In an adult this can be performed easily in the office setting. This is often impossible in children, thus they are returned to the operating room two weeks post operatively for cleaning of the opera-

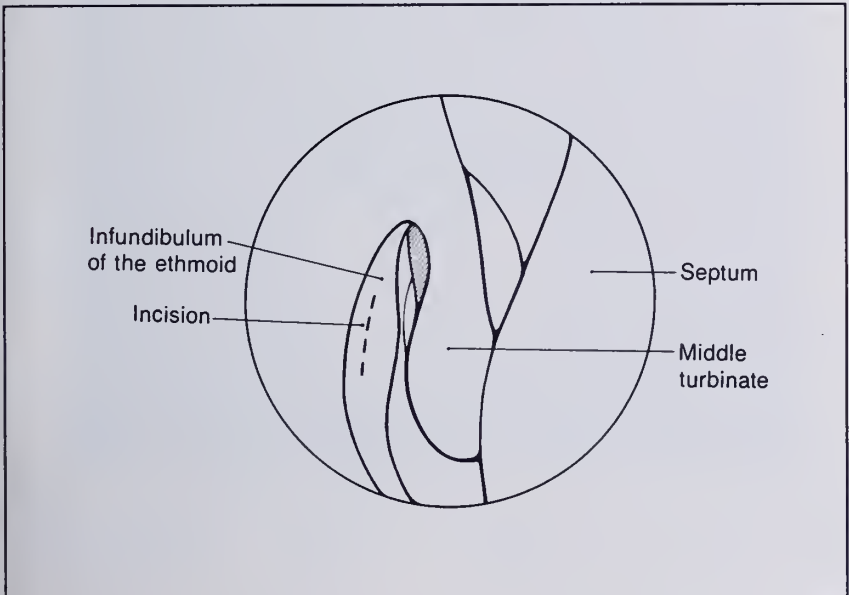


Figure 3 - Initial incision to enter the ethmoid sinuses.

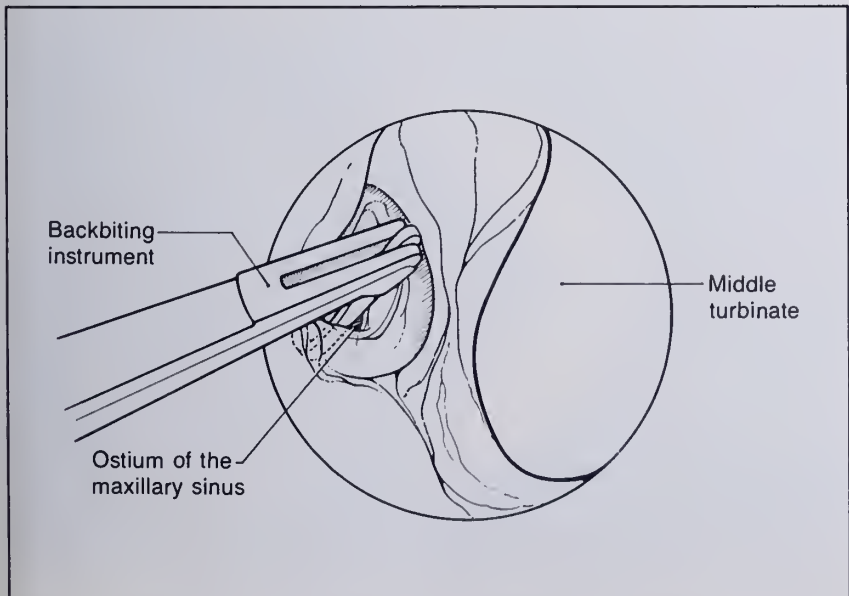


Figure 4 - Use of back biting forceps to enlarge the maxillary sinus ostium.

tive sites. Unless there are concerns regarding exacerbation of patient's asthma or some other medical problem, the surgeries are usually performed as an outpatient. Patients who live more than 40 miles from the hospital are observed overnight as a 23 hour outpatient, stay with friends in the immediate vicinity, or stay in a local hotel.

Potential complications include those associated with other types of surgery, such as anesthetic allergy, bleeding, and post-operative infection. Specifically the patient's parents are counseled about potential complications such as damage to the orbit, visual changes, spinal fluid leak, meningitis, and damage to the nasolacrimal duct leading to epiphora.

## RESULTS

To evaluate the results of FESS, a questionnaire similar to that used by Gross et al was mailed to the parents of each patient.<sup>11</sup> Twenty-five of the questionnaires were completed and returned. Results for the other 19 children were obtained by telephone interview. The questionnaires were completed on average 7.4 months after surgery (range one month to 21 months). Table I indicates that 86% of the children were im-

proved based on the observations of their parents. Improvement was judged by reduced symptoms, reduced antibiotic use, and the need for fewer doctor visits during the followup period. Thirty-three (75%) of the families would opt for FESS if asked to make the decision again. Examining the four children whose parents would not opt for surgery again, two of the children had shown no improvement, but the other two were clinically better. Of the seven families who were uncertain about having FESS if again presented with the options, four children were improved, one showed no improvement, and two families were uncertain whether there had been improvement.

## DISCUSSION

The techniques of FESS, which emphasize the restoration of normal physiologic function, were initially utilized in adults, but this experience is now being broadened to include children. The major differences in children concern their small anatomic size and the realization that the maxillary and ethmoid sinuses are often the only sinuses yet pneumatized. These differences are especially true in infants and require that the surgeon be skilled in the technique.

Although most children with sinusitis respond to aggressive medical management, the underlying cause for the disease is often unclear. It has been reported that allergic disease is associated with sinus diseases in a large percentage of pediatric patients.<sup>14</sup> Smaller numbers of children with sinusitis have immunologic defects, ciliary motility disorders, or systemic problems such as cystic fibrosis. None of our children were known to have any of these problems. Likewise, no anatomic problems such as polyps, severely deviated septa, tumors, or hugely hypertrophied turbinates were found at surgery or identified on CT scan. Since many of our children attended preschool or daycare, it may be that recurrent viral URI's were the inciting event for their disease.

Medical management of pediatric sinusitis generally includes 4-6 weeks of antibiotics, oral decongestants, and often intranasal steroids. In the allergic patient, environmental control and immunotherapy may also be useful. Most treatment failures seem to stem from using an inappropriate antibiotic or not using a proper antibiotic long enough. All patients in this study had received at least 5 weeks of antibiotics with 86% of them (38 of 44) having received more than 10 weeks.

Patients who do not respond to medical management may be candidates for FESS. A coronal sinus CT scan is required before surgery to provide a detailed view of the sinuses and the ostiomeatal complexes (see Figure 5). In our patients, the maxillary sinuses were involved in 100% with the ethmoid also involved in many. One or both

Table I

Has FESS helped your child's sinus problems?		
Yes	38	(86%)
No	3	(7%)
Maybe	3	(7%)
Would you choose to have this surgery again?		
Yes	33	(75%)
No	4	(9%)
Maybe	7	(16%)





Figure 5 - Representative scan of a child with sinusitis. Open arrows indicate obstructed ostiomeatal complexes. Dark arrow shows grossly thickened maxillary mucosa.

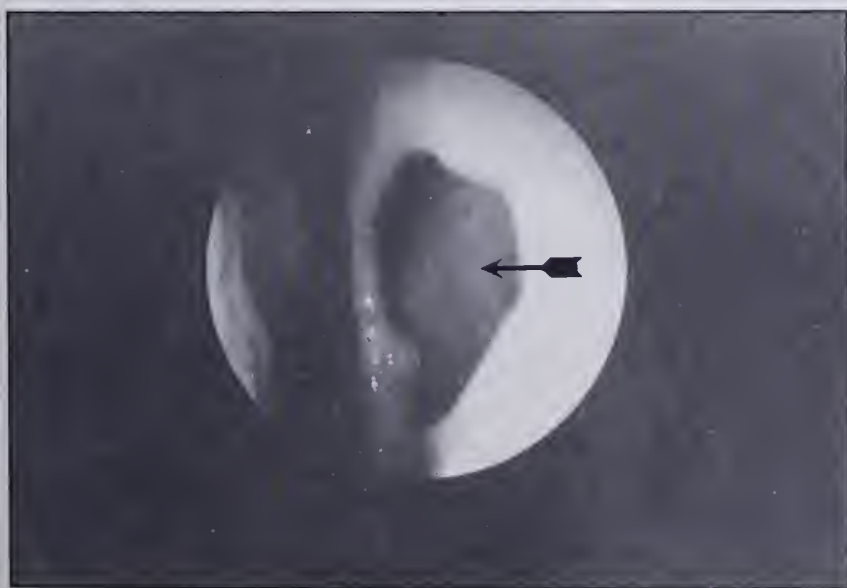


Figure 6 - Widely patent maxillary sinus ostium as seen on follow-up.

ostiomeatal complexes were obstructed in 100%. In each case the combination of chronic symptoms, incomplete response to medical treatment, and an abnormal sinus CT scan led to the recommendation for FESS.

In our study, 86% of the children were improved after FESS. Likewise, 85% of the children less than 6 years of age were improved. In addition, there were no anesthetic or surgical complications in any of the children. These results compare favorably with the findings Gross et al reported in 1989. In this earlier study of 57 older children (range 3-15 years) with chronic or recurrent sinusitis, 92% were improved after FESS.

In our relatively short follow-up period (mean of 7.4 months), the patients did well with a decrease in symptoms and the need for the medications. Figure 6 shows a widely patent maxillary sinus ostium several months after surgery. It is noteworthy that virtually all the asthmatic patients had a subjective improvement in their asthma. Although longer followup is needed, these findings are certainly encouraging.

In summary, chronic sinus disease in children can be a difficult-to-control problem. The advent of FESS offers a more physiologically sound technique to address patients that do not respond to medical management. In skilled hands, this technique is associated with few complications and appears to offer symptom relief even in young patients. □

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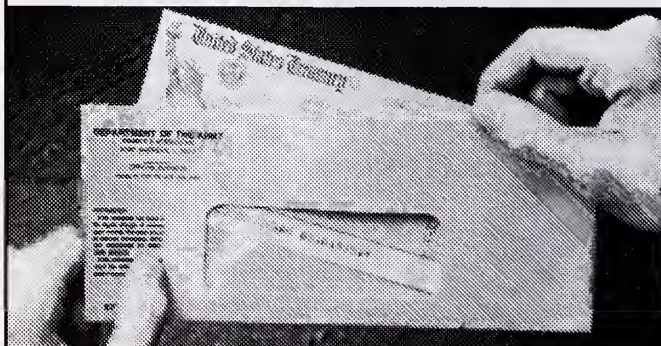
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**Dr. Haltom** is in the practice of allergy and immunology with the Mississippi Asthma and Allergy Clinic, P.A. and **Dr. Cannon** is in the practice of Otolaryngology, with the Head and Neck Surgical Group.

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# Evaluation of Mammographic Stellate Lesions

W. MEL. FLOWERS, JR., MD  
CYNTHIA I. POWERS, MD

*Editorial Note: This article is a reprint from the October 1992 issue. In the original publication the photos for figures 1 and 2 were swapped.*

**P**Primary breast carcinoma classically presents as an ill-defined mass on mammography. Frequently, there will be a central density with radiating spicules. Gross examination of these tumors reveals a firm, white, gritty center with tendrils radiating into the adjacent breast tissue. The result of mammography is a stellate mass, a lesion that once detected, has a high positive predictive value for malignancy.

The stellate mass is only one of several different radiographic signs that alert the radiologist that there may be a malignancy present. The signs also include a circumscribed mass, skin thickening, nipple retraction, a newly developing density, an asymmetrical density, ductal dilatation, architectural distortion, and abnormal calcification. The present discussion will be limited to the evaluation of the stellate mass.

## DETECTION

Perception of the stellate lesion may actually be a greater problem than analysis. It may be much more difficult to find the abnormality

than to decide what to do about it. The breasts are composed of fibroglandular tissue that can be quite dense. This normal tissue can obscure lesions. Confluent strands of fibroglandular tissue can also mimic a stellate lesion, suggesting an abnormality where none exists. These pseudolesions can be differentiated with compression spot films.

Nowhere in radiology is meticulous attention to technique more important than in mammography. The patient must be properly positioned. The films must be properly exposed. The films should be developed with a dedicated or modified automatic processor that extends the time in the developer to increase the contrast of the study. Quality control must be a daily concern. No amount of skill can properly compensate for poor quality films.

Once high quality radiographs have been produced, there are additional factors that can improve the detection rate. Viewing conditions must be given serious consideration. There should be a low amount of ambient light in the

room. Even more important, the film should be properly masked so that stray light from the view box does not reach the eyes. These simple but highly important details should not be neglected; they considerably improve the ability to perceive lesions.

If older mammograms are available, critical comparison will sometimes reveal a developing density: a new lesion or a lesion getting larger with time. The change, or even the density itself may not be properly appreciated with only the current study.

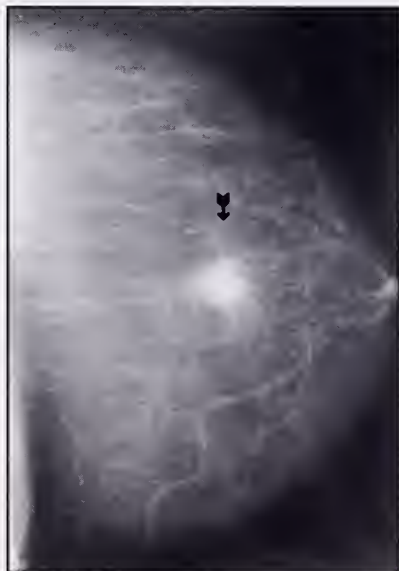
The mammograms should be properly hung on the view box so the mirror images are compared: right vs. left if only the single study is available; old vs. new if there are previous films. Then a systematic critical comparison should be made with and without a good magnifying glass.

## ANALYSIS OF THE STELLATE MASS

Once a stellate mass is detected, radiological diagnosis can be highly accurate. Not all stellate lesions are malignant, but almost all will

require biopsy. A stellate lesion consists of a center and a radiating structure.

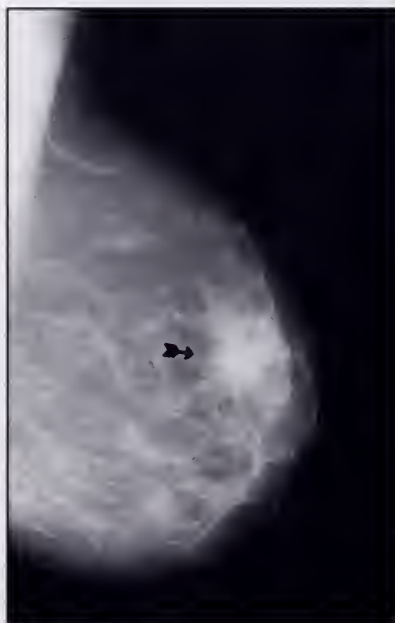
A malignant stellate lesion such as scirrhous carcinoma (infiltrating duct carcinoma) has a distinct central tumor mass and sharp dense radiating lines of variable length. Two benign lesions that can present as stellate lesions are traumatic fat necrosis and radial scar. The center of these benign lesions usually lacks a solid dense central tumor mass proportional to the length of these spicules. Also, the spicules are of lower density than in carcinoma. The spicules of a radial scar occur in multiple bunches; those of carcinoma are more random. Both carcinoma and fat necrosis can be associated with localized skin thickening and retraction; radial scars are not. The radiographic appearance of carcinoma is constant from projection to projection; the radiographic appearance of the benign lesions may change from projection to projection. The history may be helpful in the differential diagnosis of traumatic fat necrosis. Other benign lesions may rarely present as a



**Figure 1 - Carcinoma.** The lesion has a very dense center. The radiating spicules are shorter than the mass.



**Figure 2 - Radial scar.** There is no central density or mass. Long spicules radiate from a relatively lucent center.



**Figure 3 - Fat necrosis.** The patient had been biopsied for benign disease five months previously. There is now a stellate mass at the biopsy site, which resembles a carcinoma.

stellate mass including hyalinizing fibroadenoma with fibrosis.

It is important to determine that a stellate lesion can be identified

on two different projections. Confluent fibroglandular tissue may simulate a stellate mass on one projection but on the orthogonal view may disperse. Spot compression views may be helpful to evaluate the central density and displace the surrounding fibroglandular tissue. Additional signs, such as architectural distortion and associated microcalcifications may suggest malignancy.

## SUMMARY

Breast masses can be classified into circumscribed masses and stellate masses. Stellate masses are more difficult to detect but are easier to analyze. Good technique, proper processing, proper viewing conditions, and critical comparison of right vs. left and current vs. old can aid in the detection of stellate masses.

Once detected, analysis is straightforward. Most will be scirrhous carcinomas. A few will be radial scars, traumatic fat necrosis, or rare benign lesions. Additional signs such as architectural distortion and microcalcifications can be very important. Additional views, including spot compression films, may be decisive.

Not all stellate lesions are malignant, but most will require biopsy. Traumatic fat necrosis may be differentiated on the basis of history or radiographic appearance and does not need intervention. Lesions suspicious for carcinoma and radial scars should be excised and examined histologically. □

**Dr. Flowers** is associate professor of Radiology and **Dr. Powers** is an assistant professor of Radiology at the University of Mississippi Medical Center.



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| January 5   | "Orthognathic Surgery"<br>Steven Gandy, D.M.D.  |
| January 12  | "Update on Addictive Disease"<br>Kenneth Cronin, M.D.   |
| January 19  | St. Dominic's Ethics Committee Presents:<br>"Current Controversies in the Right to Life / Right to Die" *<br>Sheila K. Gottschalk, M.D. ,<br>Associate Professor of Pediatrics, L.S.U. School of Medicine |
| January 26  | "Schizophrenia"<br>J. E. Ruff, M.D.   |
| February 2  | "Panic Disorders"<br>Andrew Bishop, M.D.  |
| February 9  | "Diabetic Retinopathy"<br>J. D. Fly, M.D.   |
| February 16 | "Medical Evaluation of the Pre-Operative Patient"<br>Ralph Sulser, M.D.   |
| February 23 | "Total Parenteral Nutrition"<br>James S. Jones, M.D.  |
| March 1     | "Coronary Heart Disease Risk Recognition and Assessment"<br>Malcolm Taylor, M.D.<br>(Educational materials developed with a grant from the Roerig Division of Pfizer)                                     |
| March 9     | "Helicobacter Pylori: Significance in Upper G.I. Disease"<br>Billy Long, M.D.   |
| March 16    | SPRING BREAK - no program   |
| March 23    | To be announced<br>Al Meena, M.D.   |
| March 30    | "Hypertensive Retinopathy"<br>Maurice James, M.D.   |

\* to also be presented at 7:30 a.m. in the hospital auditorium and again at the regular Tuesday Clinical Conference. A continental breakfast will be served in the Campbell room at 7:00 a.m.

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## For Your Benefit

### AMA Key Policies Include In PRO Program

Success! Throughout 1992, the AMA's Board of Trustees, Council on Medical Service, and AMA staff have combined to play a critical role reshaping the PRO program to embrace key AMA policy. In the Fourth Scope of work, starting April 1, 1993, HCFA will:

- replace the existing Quality Intervention Plan "point system" with a more "educational" Quality Review Process;
- require physician reviewers to be licensed in the state where the services are performed and to routinely care for Medicare beneficiaries;
- compel PROs to actively use

practicing consultants in relevant specialties when drafting new review criteria or changing existing criteria, and to consider comments from state medical associations in formulating criteria;

- for the *first* time, require PROs to allow physicians to ask for reconsideration of final notice of a quality concern determination;
- charge PROs to assess the potential impact on physician reviewers if their names are released to the physicians being reviewed; and
- minimize case-by-case review in favor of pattern analysis.

### AMA "Waived" Advocacy Lightens Lab Burdens

The CLIA Advisory Committee unanimously recommended that the minimally regulated "physician performed" category of clinical laboratory tests be established. This category of testing was vigorously advocated by both the AMA and twenty

two specialty societies. The CDC is expected to accept the recommendation, also supported by HHS Secretary Louis Sullivan, MD. The AMA will meet with the CDC to discuss types of tests to be included in the "physician performed" category.



### Delegate's Report

## 1992 AMA Interim Meeting Of The House of Delegates

- **The AMA House of Delegates met in Nashville, TN, December 6-9, 1992.**
- **The House considered 231 resolutions and 90 Board and Council reports** on a wide variety of national issues of critical importance to the future practice of medicine and the future health and well-being of the American people.
- **There were 436 delegates seated.**
- **The House composition is:**  
343 delegates representing state medical associations  
83 delegates representing national medical specialty societies  
10 delegates representing medical students, resident physicians, hospital medical staffs, medical schools, young physicians, Army, Air Force, Navy, United States Public Health Service, and the Veterans Administration.

#### Health System Reform

The House of Delegates considered eight reports and a number of resolutions addressing the issues surrounding health system reform. These issues such as managed care, managed competition, negotiations, global budgeting, and refinements to AMA's Health Access American dominated the time and attention of the delegates.

The House adopted a large body of policy decisions designed to guide the AMA's activities in the coming months under the new Clinton Administration.

With regard to organized medicine's role in health care policy development and implementation, the House amended and adopted the following recommendations:

1. That the AMA continue its aggressive leadership campaign for antitrust relief and legal and legislative recognition of physician's right to negotiate.

2. That the AMA continue to position the Association to provide rapid, judicious, and ef-

fective actions and responses regarding negotiating roles that allow physicians to protect the interests of patients and legitimate interests of their own.

3. That the AMA commit itself to the establishment of mechanisms to fulfill essential standards setting roles necessary to assure the quality and cost effectiveness of medical services provided through public and private health plans and, where appropriate, invite other organizations (such as, national medical specialty societies, or provider trade associations, associations of private payers, government agencies or public interest groups) to participate in these mechanisms.

4. That the AMA support the creation of a national health advisory body or task force that will form a public/private partnership with the AMA to formulate policy and implement activities in areas except for global budgets, expenditure targets or payment determinations.

5. At a time of the potential

for imminent health system reform the House of Delegates empower the Board of Trustees to act on behalf of the Association to promote proactively and negotiate for those elements of health system reform which they feel will best represent the interests of patients and the profession.

### **Managed Care -- Policy and Initiatives.**

The House considered a major report on managed care that summarized key policy assumptions underlying managed care, presented physician, purchaser, and patient perspectives on managed care, and described the current environment with respect to the inclusion of managed care in health system reform proposals.

### **Managed Competition**

In related action, the House amended and adopted a number of recommendations addressing a new term "managed competition" that frequently enters the debate on health system reform.

### **Negotiations Issue - Current Activities**

In responding to a resolution at the 1992 Annual Meeting, the Board of Trustees reviewed three initiatives recommended by the Board to: (1) enhance the involvement of physician organizations in the Medicare program; (2) enhance the involvement of physician organizations in existing private health care plans, especially managed care plans and local integrated care networks; and (3) enhance AMA activities in self-regulatory standard setting and enforcement.

### **Global Budgeting in Health System Reform Proposals**

The Board of Trustees submitted a forceful report that expressed strong opposition to a national ceiling on health care spending otherwise known as "global budgeting."

### **Health Access America - Policy Refinements**

The Board and the House of Delegates continue to modify AMA's own reform proposal called "Health Access America." The Board submitted a report that addressed issues contained in nine resolutions from the 1992 Annual Meeting calling for various refinements in the proposal.

### **Physician Ownership of Medical Facilities (Conflicts of Interest - Self Referral)**

The House of Delegates reconciled an apparent discrepancy between the Council on Ethical and Judicial Affairs policy and a resolution adopted at the last meeting by (1) reaffirming the Council's guidelines on Conflicts of Interest: Physician Ownership of Medical Facilities, and (2) rescinding the earlier resolution.

In addition the House requested CEJA to continue to study and revise these guidelines as changes in the health care system may require, considering some suggested guidelines from the College of Legal Medicine.

*(Editorial Note: The full text of this opinion is printed on page 19 of this issue under "Current Opinions" of the Council on Ethical and Judicial Affairs of the American Medical Association.)*

### **Primary Care**

The House received several

resolutions that addressed the need for increased production of primary care physicians. The AMA has existing policy committed to this objective and has undertaken initiatives to solve this growing problem and expects to submit a report with recommendations in six months.

### **National Practitioner Data Bank "Self-Query"**

The Board of Trustees submitted a report reviewing current policy on the confidentiality involved in a "self-query" by a practitioner from a data bank report.

Listed below are some other actions that seemed to generate unusual interest among members of the House or the public media:

SI Units of Measure, Autologous Blood Transfusions, Inappropriate Federal Prosecution, Family Violence, Adequacy of Sterilization in Commercial Enterprises, Baby Walkers, Professional Liability Issues, CLIA'88 Regulations, Unified Meeting, Caring for the Poor, and AMA Budget.

Your MSMA Delegates and Alternate Delegates to meetings of the AMA House of Delegates stand ready to discuss with you any actions of the House you desire further information about. They are: Delegates - **Drs. Sidney O. Graves**, Natchez; **J. Edward Hill**, Hollandale; **James C. Waites**, Laurel; **J. Elmer Nix**, Jackson; and **William C. Gates**, Columbus. Alternate Delegates - **Drs. Fred McMillan**, Alton B. Cobb, W. Lamar Weems, Jackson; **Candace E. Keller**, George McGee, Hattiesburg; and **W. Joseph Burnett**, Oxford. □

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## **The President's Page**

**WILLIAM C. GATES, MD**

### **A TRIBUTE TO CARL EVERS**

**E**very so often in the protoplasmic continuum a truly exceptional individual appears and creates a brilliant and beautiful glow on the horizon of our lives.

Such a man was Carl Evers. His value to us personally and professionally will be repeatedly punctuated by his absence.

His service as a bridge well-traveled between *academia* and organized medicine is well known and virtually irreplaceable.

He gave much of himself as an academician... teacher, consultant and administrator... as well as a confidant in things philosophical. His opinion was highly respected and is sorely missed.

Carl found joy in many things, large and small, not the least of which were his family, his friends and his calling. He knew and we know that his beloved wife, Jan, was the wind beneath his wings.

His view of life was always tempered by his irrepressible sense of humor which was one of his most revealing and enduring attributes.

He has guaranteed his immortality because he was the kind of man who will live on in the minds and memory of all those who knew and loved him.

We, as the living, can pay tribute daily to Carl by celebrating and emulating his virtues. It will serve us well in these troubled times for our profession - and it will please Carl to know that he is continuing to contribute to our efforts, even though he has "crossed the bar," as Tennyson put it. We will miss him immensely.

Hail and farewell, Carl!

*(Continued on page 16)*



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# Editorials

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JOURNAL OF THE  
MISSISSIPPI STATE  
MEDICAL ASSOCIATION  
VOLUME XXXIV, NUMBER 1  
JANUARY 1993

## Medicine In 1993

As 1992 draws to a close we stop to mentally review our accomplishments and shortcomings, both personally and professionally. We then begin to fully prepare ourselves to confront the future... the upcoming year of 1993.

Professionally the new year promises to present many challenges and unknowns. The electronic and print media are alive with requests from political groups, businesses and special interest forces for sweeping changes in the health care delivery system. Additionally, a new administration will arrive in Washington with its own agenda, which will be impacted by the input of the other groups.

It now appears that there will be significant changes in the way medicine is practiced in this country. This will come as a shock to many in the medical field but there will be changes and medicine will not continue as it has in the past.

The uninsured and under-insured, as well as the poor are a reality. Unfortunately these are social problems that have far outgrown the capability of medicine to voluntarily pick up the slack by personally treating such indigent and uninsured at no charge. Economic realities prohibit any physician from providing a large amount of such services and still remain viable as a business, and medicine has surely become a major business.

Medicine is no longer looked upon as a service. Aggressive business modalities have entered the medical market place, replacing the traditional services offered in the past. Superimposed upon all of this is the serious national debt and current budgetary problems. Although medicine is not totally responsible for these problems, any attempt to resolve them is going to directly affect all of us.

While many physicians will violently resist such changes, it is a reality that the current system has not provided for the medical necessities of our total society. It will not matter that many of the changes are the result of social and political changes in the society. Whatever is done to address these problems will heavily impact all of medicine.

Currently it appears that our best option is to do as all the other forces and make a forceful presentation of our thoughts and recommendations through our societies and hope that a favorable impact can be made, and in turn help in the restructuring of medicine. Proposing a continuation of the current system will be no longer tolerated or respected. New and innovative ideas are required. This cannot be done by individual physicians and will require an organized effort. So please come forward with your ideas and support. Be a part of the action in guiding medicine through these times.

**Myron W. Lockey,**  
Editor

The editorial opinions expressed in this Journal are those of the indicated author. Editorial opinions are not expressions of the views, or official policies of The Mississippi State Medical Association. We encourage the membership to submit letters for publication regarding any opinion expressed or information contained in the Journal.

## **Requiem For Carl**

Hail and farewell, Carl!  
We raise our glass to honor you, old friend.  
Although we deplore your  
Premature "crossing of the bar,"  
We acknowledge a Divine Wisdom,  
Incomprehensible to us mortals,  
And the omniscience and omnipotence  
Steering our frail ships on a stormy sea of uncertainty  
But traveling between those certain buoys of birth and death.  
While we struggle with our own grief,  
We attempt to comprehend the grieving of your family,  
Finding solace in the celebration of your life  
And in the emulation of your virtues,  
Realizing your immortality is assured  
In the minds and memories of us all.  
You will be remembered as a physician's physician  
And as a kind and sensitive human being  
Who lived and loved well.  
Now, as Gaius Catullus said in ancient times,  
We say, "And forever, O my brother,  
Hail and farewell."

**Bill Gates**

*(Editor's note - Dr. Carl Gustav Evers, a native Minnesotan, received his MD degree from the University of Minnesota in 1959. He elected to do his post graduate training in pathology at the University of Mississippi Medical Center and joined the faculty upon concluding his residency in 1964. In 1973 he was named Assistant Dean for Student Affairs and in 1978 he became Associate Dean for Academic Affairs, a post he held until his untimely death. Carl*

*was an early and active participant in organized medicine at the local, state and national level. In the process he achieved a number of "firsts".*

*At age 37, Carl was the youngest physician ever elected to the MSMA Board of Trustees, and the youngest person ever elected as the Association's President. He was the first University of Mississippi Medical School full-time faculty member to serve on the Association's board and as Presi-*

*dent. All of these marvelous achievements were crowned by one of Carl's finest moments in June, 1991, when he became the first Mississippian ever elected by the AMA House of Delegates to one of its councils, the prestigious Council on Medical Education.*

*Carl is survived by his wife, Jan and children, Karen, Julie and Gus.*

*His flame will eternally burn bright, fueled by the love of his colleagues and friends.) □*

# Letters

To: Joseph M. Johnston, MD  
Associate Editor, *Journal*  
*MSMA*

I was pleased to see your comments in the editorial column of the November *Journal Of The Mississippi State Medical Association*. I certainly agree with you with regard to your comments on media managed politics. I think another problem that has surfaced is industry driven technology. We embrace various technologies based on the enthusiasms generated by the industry producing the technology, and not the clinical enthusiasm of our colleagues who have used the technology and found it better than the existing methods.

We do have the best health care system in the world. Support of a genre of physicians and facilities whose only interest is "the bottom line" will probably bring down on us enough regulation and change that only those who are clever enough to maintain their "economic credentials" will survive.

Sincerely,  
Toxey M. Morris, MD  
Hattiesburg, MD

# YOCON<sup>®</sup> YOHIMBINE HCl

**Description:** Yohimbine is a 3a-15a-20B-17a-hydroxy Yohimbine-16a-carboxylic acid methyl ester. The alkaloid is found in Rubaceae and related trees. Also in Rauwolfia Serpentina (L) Benth. Yohimbine is an indolalkylamine alkaloid with chemical similarity to reserpine. It is a crystalline powder, odorless. Each compressed tablet contains (1/12 gr.) 5.4 mg of Yohimbine Hydrochloride.

**Action:** Yohimbine blocks presynaptic alpha-2 adrenergic receptors. Its action on peripheral blood vessels resembles that of reserpine, though it is weaker and of short duration. Yohimbine's peripheral autonomic nervous system effect is to increase parasympathetic (cholinergic) and decrease sympathetic (adrenergic) activity. It is to be noted that in male sexual performance, erection is linked to cholinergic activity and to alpha-2 adrenergic blockade which may theoretically result in increased penile inflow, decreased penile outflow or both.

Yohimbine exerts a stimulating action on the mood and may increase anxiety. Such actions have not been adequately studied or related to dosage although they appear to require high doses of the drug. Yohimbine has a mild anti-diuretic action, probably via stimulation of hypothalamic centers and release of posterior pituitary hormone.

Reportedly, Yohimbine exerts no significant influence on cardiac stimulation and other effects mediated by B-adrenergic receptors, its effect on blood pressure, if any, would be to lower it, however no adequate studies are at hand to quantitate this effect in terms of Yohimbine dosage.

**Indications:** Yocon<sup>®</sup> is indicated as a sympatholytic and mydriatic. It may have activity as an aphrodisiac.

**Contraindications:** Renal diseases, and patient's sensitive to the drug. In view of the limited and inadequate information at hand, no precise tabulation can be offered of additional contraindications.

**Warning:** Generally, this drug is not proposed for use in females and certainly must not be used during pregnancy. Neither is this drug proposed for use in pediatric, geriatric or cardio-renal patients with gastric or duodenal ulcer history. Nor should it be used in conjunction with mood-modifying drugs such as antidepressants, or in psychiatric patients in general.

**Adverse Reactions:** Yohimbine readily penetrates the (CNS) and produces a complex pattern of responses in lower doses than required to produce peripheral a-adrenergic blockade. These include, anti-diuresis, a general picture of central excitation including elevation of blood pressure and heart rate, increased motor activity, irritability and tremor. Sweating, nausea and vomiting are common after parenteral administration of the drug.<sup>1,2</sup> Also dizziness, headache, skin flushing reported when used orally.<sup>1,3</sup>

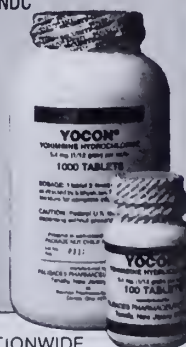
**Dosage and Administration:** Experimental dosage reported in treatment of erectile impotence.<sup>1,3,4</sup> 1 tablet (5.4 mg) 3 times a day, to adult males taken orally. Occasional side effects reported with this dosage are nausea, dizziness or nervousness. In the event of side effects dosage to be reduced to 1/2 tablet 3 times a day, followed by gradual increases to 1 tablet 3 times a day. Reported therapy not more than 10 weeks.<sup>3</sup>

**How Supplied:** Oral tablets of Yocon<sup>®</sup> 1/12 gr. 5.4 mg in bottles of 100's NDC 53159-001-01 and 1000's NDC 53159-001-10.

## References:

1. A. Morales et al., New England Journal of Medicine: 1221, November 12, 1981.
2. Goodman, Gilman — The Pharmacological basis of Therapeutics 6th ed., p. 176-188. McMillan December Rev. 1/85.
3. Weekly Urological Clinical letter, 27:2, July 4, 1983.
4. A. Morales et al., The Journal of Urology 128: 45-47, 1982.

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Dr. Elizabeth Keeling is a Board Certified Pediatrician practicing in Jackson, Mississippi.



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# **"Current Opinions"**

## **of the Council on Ethical and Judicial Affairs of the American Medical Association**

### **OPINIONS ON PRACTICE MATTERS**

#### **C**onflicts Of Interest: Health Facility Ownership By A Physician

Physician ownership interests in commercial ventures can provide important benefits in patient care. Physicians are free to enter lawful contractual relationships, including the acquisition of ownership interests in health facilities, products, or equipment. However, when physicians refer patients to facilities in which they have an ownership interest, a potential conflict of interest exists. In general, physicians should not refer patients to a health care facility which is outside their office practice and at which they do not directly provide care or services when they have an investment interest in that facility.

There may be situations in which a needed facility would not be built if referring physicians were prohibited from investing in the facility. Physicians may invest in and refer to an outside facility, whether or not they provide direct care or services at the facility, if there is a demonstrated need in the community for the facility and alternative financing is not available. Need might exist when there is no facility of reasonable quality in the community or when use of existing facilities is onerous for patients. In such cases the following requirements should also be met: (1) physicians should disclose their investment interest to their patients when making a referral, provide a list of effective alternative facilities if they are available, inform their patients that they have free choice to obtain the medical services elsewhere, and assure their patients that they will not be treated differently if they

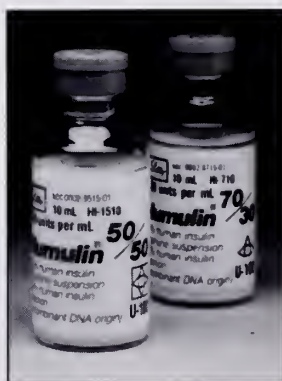
do not choose the physician-owned facility; (2) individuals not in a position to refer patients to the facility should be given a bona fide opportunity to invest in the facility on the same terms that are offered to referring physicians; (3) the opportunity to invest and the terms of investment should not be related to the past or expected volume of referrals or other business generated by the physician investor or owner; (4) there should be no requirement that a physician investor make referrals to the entity or otherwise generate business as a condition for remaining an investor; (5) the return on the physician's investment should be tied to the physician's equity in the facility rather than to the volume of referrals; (6) the entity should not loan funds or guarantee a loan for physicians in a position to refer to the entity; (7) investment contracts should not include "noncompetition clauses" that prevent physicians from investing in other facilities; (8) the physician's ownership interest should be disclosed to third party payers upon request; (9) an internal utilization review program should be established to ensure that investing physicians do not exploit their patients in any way, as by inappropriate or unnecessary utilization; (10) when a physician's commercial interest conflicts to the detriment of the patient, the physician should make alternative arrangements for the care of the patient. □



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# Medical Organization

## Dr. Cobb Retires After Almost 20 Years As State Health Officer

State Health Officer Dr. Alton B. Cobb retired from his position with the Mississippi State Department of Health effective December 31. Dr. Cobb submitted his letter of resignation to the State Board of Health and announced his decision to staff members November 16.

Dr. Cobb began his public health career as county health officer in Sunflower County in 1957. Before becoming state health officer in 1973, he served as director of the Mississippi Medicaid Commission for almost four years.

In November, Dr. Cobb was awarded the American Public Health Association's Award for Excellence in recognition of his "exceptionally meritorious contributions to the improvement of the health of the people. It honors creative work of particular effectiveness in applying scientific knowledge or innovative organizational work to the betterment of community health."

Under Dr. Cobb's leadership, the Mississippi State Department of Health moved to the district management system for county health departments to improve

strength and efficiency of service delivery. Mississippi pioneered integration of services at county health departments, a major departure from the traditional categorical service delivery system.

Dr. Cobb also led Mississippi's public health system in introducing a policy for fee collections for public health services based on the patients' ability to pay and the billing of Medicaid and other third party payment sources for services. Over the past several years, these sources of funding have provided support of the statewide system of preventive services despite state funding cutbacks.

Other gains during Dr. Cobb's tenure include the nationally-recognized Mississippi WIC Program, reduced infant mortality, modernized public health statutes, compulsory school immunizations, a statewide emergency medical services system, and expansions in environmental health.

Dr. Cobb said, "I extend to all my colleagues in the Mississippi Public Health system my appreciation for the important work

they perform for all Mississippians.

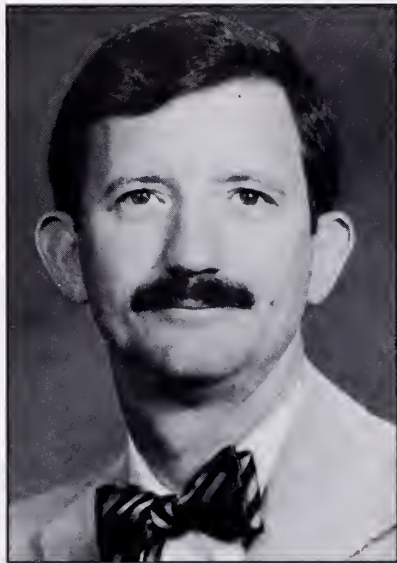
"I will forever remain a loyal alumnus of the team and a supporter of the State Department of Health and its staff throughout the state," he said.

State health authorities, interviewed for a *Clarion-Ledger* article, agreed the Dr. Cobb's tenure and contributions to public health have been outstanding.

Dr. Aaron Shirley, director of the Jackson-Hinds Comprehensive Health Center, said "His certainly will be some big shoes to fill," a statement echoed by several Jackson-area media in related editorials.

"His legacy will remain a very positive note in the state's health history for years to come," said Dr. Norman Nelson, vice chancellor for health affairs, University Medical Center. □

## Dr. John McGraw Elected President of Medical-Dental Fellowship



John J. McGraw, MD, an orthopaedic surgeon in Laurel, has been elected president of the national Baptist Medical-Dental Fellowship.

Dr. McGraw took office at the 16th annual meeting of the fellowship, held in November in Memphis, Tennessee. He will serve a one-year term.

The Baptist Medical-Dental Fellowship is a medical missions organization established to support Southern Baptist missionary doctors serving all over the world. The BM-DF encourages short-term volunteer medical

missions service by professionals based in the United States.

A recent project in Ladakh, India involved eight doctors, four nurses and support personnel who "camped out" at an average altitude of 13,000 feet in the Himalayas and provided medical services for 12 villages accessible only two months out of the year. They saw more than 3,000 patients, none of whom had ever seen a doctor before.

Headquarter in Memphis, the fellowship has more than 1,750 physicians and dentists for 43 states and seven foreign countries. Some 600 of these take part in volunteer medical missions work in the United States and overseas every year. □

## Dr. George Abraham Presents Workshop On Patient Education

Dr. George E. Abraham, II and Miriam Jabour, marketing director of The Vicksburg Family Medicine Clinic, P.A. presented a workshop titled *Patient Education: Good Medicine and Good Marketing* at the 14th Annual Conference on Patient Education.

The conference, sponsored annually by The Society of Teachers of Family Medicine and The Academy of Family Physicians, is attended by family physicians, psychologists, faculty and residents from various family medicine residency program in the United States and Canada, nurse educators, dietitians and others involved in some aspect of patient education.

*Empowering The Patient*, the conference theme was highlighted throughout the twenty-

five in-depth workshops. Key-note presentations were made by Judith Ribble, PhD, director of Continuing Medical Education for Lifetime Medical Television and Nancy Dickey, MD, a family physician and current member of the AMA Board of Trustees and Council on Ethical and Judicial Affairs.

The conference emphasized practical skills, interdisciplinary interaction and team development, and new approaches to educating patients about specific health problems.

Dr. Abraham, a Board Certified Family Physician with a Certificate of Added Qualifications in Geriatrics, received his MD from The University of Mississippi School of Medicine where he also completed his Residency in Family Medicine.

He is a member of AAFP, West MS Medical Society, MSMA, Associate Editor of *The Journal Of The Mississippi State Medical Association*, AMA, Board Member and Treasurer of the MFMC and a Board Member of The Vicksburg Medical Center. Dr. Abraham was a co-recipient of The 1989 *Patient Care Award* for Excellence in Patient Education with Doctors Sandra F. Burford, Lee Giffin and Hildon H. Sessums, Jr., also in practice at The Vicksburg Family Medicine Clinic.

Mrs. Jabour received her degree in marketing from Southern Methodist University in Dallas, TX and has been employed as Marketing Director for the clinic for the past six years. A member of The American Marketing Association and The Academy For Health Services Marketing, she also is a partner in Medical Marketing Unlimited. □

## **MSMA Board of Trustees and Officers Meet**

MSMA's Board of Trustees and Officers held their Fall meeting in Jackson, December 12th and considered a broad range of topics including the following:

- **Adoption of a 1993 Strategic Plan** which stresses goals and activities to address health care reform, membership recruitment, strengthening MSMA component societies and practice management.
- **Review and adoption of 1993 budgets** for the association and its subsidiaries.
- **Adoption of a 1993 state health legislation program.**
- **Adoption of a statement on home health care services.**
- **Review of a Medicaid Case Manager Program.**
- **Review of planning for the 1993 MSMA Annual Session and a study of annual session format changes.**
- **Review of annual reports from the MS Board of Medical Licensure, MSMA Impaired Physicians Committee, MS State Department of Health, MS Foundation for Medical Care and Medical Assurance Company of MS.**
- **Review of MSMA Auxiliary activities.**

Attending the Fall meeting were the following officers: **William C. Gates, MD**, Columbus, President; **Mrs. Kathy Carmichael**, Hattiesburg, MSMA Auxiliary President; **Don Q. Mitchell, MD**, Jackson, President-Elect; **Stanley Hartness, MD**, Kosciusko, Secretary-Treasurer; **Myron W. Locky, MD**, Jackson, Editor, *Journal MSMA*; **Sidney O. Graves, MD**, Natchez, AMA Delegate; **Alton B. Cobb, MD**, Jackson, AMA Delegate; and **James C. Waites, MD**, Laurel, AMA Delegate.

Board of Trustees members were: **Mal G. Morgan, MD**, Natchez, (District 7) Chairman; **Fred L. McMillan, MD**, Jackson, (District 4) Vice Chairman; **Eric E. Lindstrom, MD**, Laurel, (District 6) Secretary; **Michael H. Carter, MD**, Greenwood, (District 1); **William A. Spencer, MD**, Oxford, (District 2); **Leonard H. Brandon, MD**, Starkville, (District 3); **Julian Henderson, MD**, Jackson, (District 4); **Dewitt G. Crawford, MD**, Louisville, (District 5); and **David L. Clippinger, MD**, Gulfport (District 8). □



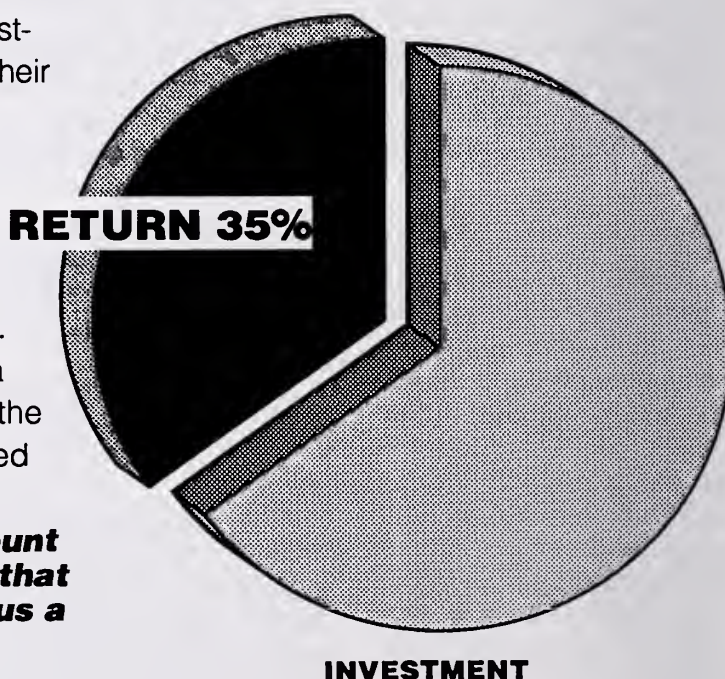
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# From the University of Mississippi Medical Center

## Dr. Ball Elected President of The American Aging Association

Dr. Sheldon Ball, an assistant professor of pathology at the University of Mississippi Medical Center, has been elected president of the American Aging Association.

Founded in 1970, the association is a national lay-scientific organization comprised of physicians, scientists and other

individuals interested in discovering more about aging and its consequences.

Dr. Ball is a graduate of the University of Miami where he received his MD in 1983. He also is a graduate of the University of California-Davis where he received a BS and PhD in chemistry.

Dr. Ball joined the Medical Center faculty in 1990. He serves on the editorial board of the *Journal of Optimal Nutrition* and is the editor of the AGE News, a publication for the American Aging Association. Dr. Ball is also a member of the association's board of directors. □

## Kenneth St. John Receives *Scientific American Award*

Kenneth St. John, associate professor of orthopedic surgery at the University of Mississippi Medical Center, has received a *Scientific American Award* from the American Society of Testing and Materials (ASTM). St. John received the award for long-term contributions to standards development in medical devices.

St. John is a member of the ASTM's medical and surgical material and device committee and serves as chairman of the ASTM biocompatibility and editorial subcommittees. He also is a member of the group's executive subcommittee and has been appointed vice chairman of the committee on publications.

ASTM is a nonprofit voluntary consensus standards organization in Philadelphia, PA.

St. John is a graduate of the Rensselaer Polytechnic Institute in Troy, NY where he received a BS in biomedical engineering. He also holds a MS in bioengineering from Clemson University in Clemson, SC. □

The Delta Region AIDS Education and Training Center grant is one of 17 federally funded for specialized comprehensive HIV/AIDS Education and Training in Arkansas, Louisiana, and Mississippi. Educational offerings are available in six disciplines - medicine, nursing, dentistry, infection control, mental health, and social work. Physicians, nurses, and health-related professionals are available to visit your area and provide educational services. Please include us in your next meeting. Additional information may be obtained by calling the Division of Infectious Diseases, University of Mississippi Medical Center.

**Jan M. Evers, RN, MN, Resource Center Director**

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# University of Mississippi Medical Center

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**Newborn Intensive Care Course (Day 1 & 2)**

January 14 ..... UMC, Jackson  
**Emergency Nursing Certification Exam Preparation**

January 14-16 ..... UMC, Jackson  
**Rigid Internal Fixation of Facial Fracture (Hand-on Course)**

January 27 ..... UMC, Jackson  
**First Line Clinical Nurse Managers Series**

January 29 ..... UMC, Jackson  
**The Dilemma: When to Return the Injured Worker to Work**

### **FEBRUARY, 1993**

February 3-4 ..... UMC, Jackson  
**Newborn Intensive Care Course (Day 3 & 4)**

February 11-12 ..... Ramada Renaissance Hotel, Jackson  
**AIDS Update 1993**

February 12 ..... UMC, Jackson  
**Cardiovascular Update 1993**

February 17 ..... UMC, Jackson  
**First Line Clinical Nurse Managers Series**

February 18-19 ..... UMC, Jackson  
**High Risk Neonatal Nursing Review and Certification Preparation**

February 26 ..... UMC, Jackson  
**Pediatric Update**

### **MARCH, 1993**

March 3-4 ..... UMC, Jackson  
**Newborn Intensive Care Course (Day 5 & 6)**

March 3 ..... Ramada Renaissance Hotel, Jackson  
**Oncology Update**

March 4 ..... UMC, Jackson  
**Oncology Nursing Review and Certification Preparation**

March 5 ..... Research and Development Center, Jackson  
**Blood Borne Parasitic Infection**

March 6 ..... UMC, Jackson  
**Nuclear Medicine**

March 10 ..... UMC, Jackson  
**First Line Clinical Nurse Managers Series**

March 12-13 ..... UMC, Jackson  
**ATLS Instructor Course**

March 23 ..... UMC, Jackson  
**Obstetrics/Newborn Update**

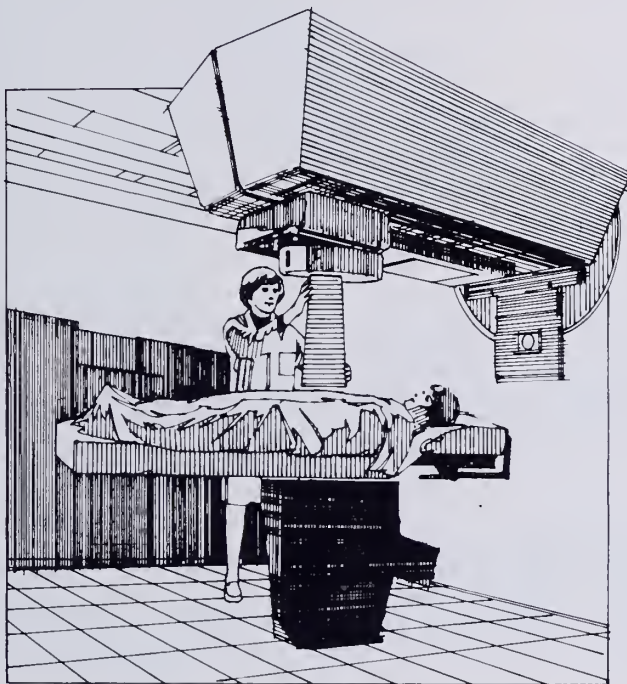
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## Personals

**Clifton C. Cartwright** of Booneville has been recertified as a Diplomate of the American Board of Family Practice.

**Craig A. Cole** of Clinton has joined the medical staff of Methodist Medical Center for the practice of general and vascular surgery.

**Donald V. Conerly** of Hattiesburg recently received board recertification as a Diplomate of the American Board of Family Practice.

**Kenneth M. Davis** has associated with North Mississippi Medical Center for the practice of gerontology, 830 South Gloster Street, Tupelo, MS.

**Harry C. Frye** of Magnolia has been recognized for 40 years of continued membership in the American Academy of Family Physicians.

**George Furr** of Clarksdale was honored with a special plaque by the Coahoma County Branch of the American Cancer Society for

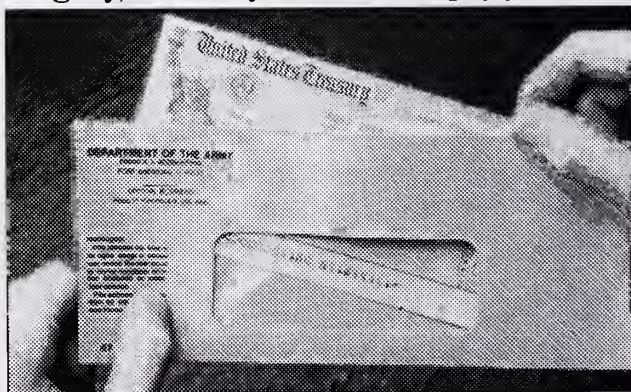
his "outstanding service in medicine and research into the effects of pesticides on body cells" in relationship to cancer and other catastrophic diseases.

**Judith G. Gearhart** of Clinton has been appointed to a three-year term on the editorial board of the *Southern Medical Journal*.

**T. Eric Hale**, of Hattiesburg recently received board recertification as a Diplomate of the American Board of Family Practice.

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## Personals/continued

**George C. Hamilton** of Jackson was elected President-elect of the Southern Psychiatric Association for 1992-1993.

**J. Edward Hill** of Hollandale was elected Chairman of the Council of the Southern Medical Association. The Council is the governing body of the Association and consist of seventeen state representatives from the SMA territory.

**Rebecca Hodges** of Kilmichael has been selected "Woman of Achievement for 1993" by the Winona Business and Professional Women's Club.

**Jeffrey A. Johnson** has associated with the Hattiesburg Clinic in the practice of internal medicine, 415 South 28th Avenue.

**Tara Scott Mallett** has associated with the Community Medical Center, Lucedale for the practice of pediatrics.

**John Evans Mann, Jr.** of Meridian, has been recertified as a diplomate of the American Board of Family Practice.

**S. Scott Massingill** of Meridian has completed the General Pediatrics Certifying Examination administered by the American Board of Pediatrics and has achieved board certification. He has also been approved for Fellowship in the American Academy of Pediatrics.

**Ray Montalvo, Jr.** has associated with The Moak-Massengill Clinic for the practice of internal medicine, 1040 Biglane Drive, Brookhaven.



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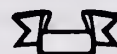
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## Physicians' Recognition Award



Two MSMA members were named recipients of the AMA Physicians' Recognition Award in November 1992. This award is presented by the American Medical Association to Physicians who have voluntarily completed a specified number of continuing medical education hours. These individuals are presented below by medical society.

Central Medical Society  
**James Douglas Fly, MD**

Prairie Medical Society  
**Robert Keith Collins, MD**

**W. J. Patterson** of Clinton has completed continuing medical education requirements to retain active membership in the American Academy of Family Physicians.

**Elizabeth N. Roy** of Vicksburg has been elected to fellowship in the American Academy of Pediatrics.

**Buddy Savoie** of Jackson lectured on disorders of the elbow and wrist and was Chief Laboratory Instructor on arthroscopy of the elbow and wrist at the AAOS Summer Institute in Seattle, Washington. He was also the featured instructor and lecturer on examination and management of disorders of the shoulder at the KIN-KOM Physical Therapy Meeting in Orlando, Florida.

**Kelly S. Segars, Sr.**, of Iuka has been named Citizen of the Year by the Iuka Chamber of Commerce for his activities in many community betterment projects and particularly for his responsibility in locating the Lockheed-Aerofjet office in Iuka.

**Robert J. Sharpton, Jr.**, of Newton, has been named a diplomate of the American Board of Family Practice.

**Valerie A. Short** announces the opening of her practice in obstetrics and gynecology, Stadium Towers, 440 East Woodrow Wilson, Suite 504, Jackson.

**Pierre F. Soucie** has associated with Columbia Family Clinic in the practice of family medicine, 502 Broad Street, Columbia.

**Keith Stanford** has associated with **Mary Anne Frank-Tarsi** for the practice of family medicine, Physicians Office Building, Grenada.

**Ed Thompson** of Jackson earned the Mississippi Public Health Association's top honor, the Felix J. Underwood Award, at their 55th Annual meeting held recently in Biloxi. He has also been appointed interim state health officer. □

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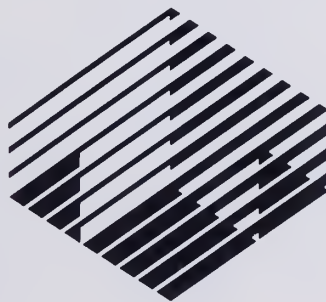
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Avanti .....	cover II
Bristol-Myers Squibb Company - Pravachol .....	covers III and IV
CancerPay Plus .....	27
CompHealth .....	30
CompuMed .....	8
Deposit Guaranty Investments .....	4
Disability Determination .....	33
Eli Lilly & Co. - Humulin .....	20
Employer Plus, Inc. ....	24
Medical Assurance Co. of MS .....	18
Medley & Company .....	31
MS Emergency Association .....	32
MS Physicians Insurance Company .....	13
MSMA Benefit Plan & Trust .....	5
Palisades Pharmaceuticals, Inc. - Yocon .....	17
Premier Printing .....	33
PRI-MED, Inc. ....	33
St. Dominic Hospital .....	9
The Doctors' Company .....	29
Trustmark .....	33
US Army Active .....	6
US Army Reserve .....	28



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hypersensitivity to any component of this medication.  
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**WARNINGS**

**Liver Enzymes:** HMG-CoA reductase inhibitors, like some other lipid-lowering therapies, have been associated with biochemical abnormalities of liver function. Increases of serum transaminase (ALT, AST) values to more than 3 times the upper limit of normal occurring on 2 or more (not necessarily sequential) occasions have been reported in 1.3% of patients treated with pravastatin in the U.S. over an average period of 18 months. These abnormalities were not associated with cholestasis and did not appear to be related to treatment duration. In those patients in whom these abnormalities were believed to be related to pravastatin and who were discontinued from therapy, the transaminase levels usually fell slowly to pretreatment levels. These biochemical findings are usually asymptomatic, although worldwide experience indicates that anorexia, weakness, and/or abdominal pain may also be present in rare patients.

As with other lipid-lowering agents, liver function tests should be performed during therapy with pravastatin. Serum aminotransferases, including ALT (SGPT), should be monitored before treatment begins, every six weeks or the first three months, every eight weeks during the remainder of the first year, and periodically thereafter (e.g., at about six-month intervals). Special attention should be given to patients who develop increased transaminase levels. Liver function tests should be repeated to confirm an elevation and subsequently monitored at more frequent intervals. If increases in AST and ALT equal or exceed three times the upper limit of normal and persist, then therapy should be discontinued. Persistence of significant aminotransferase elevations following discontinuation of therapy may warrant consideration of liver biopsy.

Active liver disease or unexplained transaminase elevations are contraindications to the use of pravastatin (see CONTRAINDICATIONS). Caution should be exercised when pravastatin is administered to patients with a history of liver disease or heavy alcohol ingestion (see CLINICAL PHARMACOLOGY: Pharmacokinetics/Metabolism). Such patients should be closely monitored, started at the lower end of the recommended dosing range, and (titrated to the desired therapeutic effect.

**Skeletal Muscle:** Rhabdomyolysis with renal dysfunction secondary to myoglobinuria has been reported with pravastatin and other drugs in this class. Uncomplicated myalgia has also been reported in pravastatin-treated patients (see ADVERSE REACTIONS). Myopathy, defined as muscle aching or muscle weakness in conjunction with increases in creatine phosphokinase (CPK) values to greater than 10 times the upper limit of normal was reported to be possibly due to pravastatin in only one patient in clinical trials (<0.1%). Myopathy should be considered in any patient with diffuse myalgias, muscle tenderness or weakness, and/or marked elevation of CPK. Patients should be advised to report promptly unexplained muscle pain, tenderness or weakness, particularly if accompanied by malaise or fever. **Pravastatin therapy should be discontinued if markedly elevated CPK levels occur or myopathy is diagnosed or suspected. Pravastatin therapy should also be temporarily withheld in any patient experiencing an acute or serious condition predisposing to the development of renal failure secondary to rhabdomyolysis, e.g., sepsis; hypotension; major surgery; trauma; severe metabolic, endocrine, or electrolyte disorders; or uncontrolled epilepsy.**

The risk of myopathy during treatment with pravastatin is increased if therapy with either cyclosporine, gemfibrozil, erythromycin, or niacin is administered concurrently. There is no experience with the use of pravastatin together with cyclosporine. Myopathy has not been observed in clinical trials involving small numbers of patients who were treated with pravastatin together with niacin. One trial of limited size involving combined therapy with pravastatin and gemfibrozil showed a trend toward more frequent CPK elevations and patient withdrawals due to musculoskeletal symptoms in the group receiving combined treatment as compared with the groups receiving placebo, gemfibrozil, or pravastatin monotherapy. Myopathy was not reported in this trial (see PRECAUTIONS: Drug Interactions). One patient developed myopathy when clofibrate was added to a previously well tolerated regimen of pravastatin; the myopathy resolved when clofibrate therapy was stopped and pravastatin treatment continued. **The use of fibrates alone may occasionally be associated with myopathy. The combined use of pravastatin and fibrates should generally be avoided.**

**PRECAUTIONS**

**General:** Pravastatin may elevate creatine phosphokinase and transaminase levels (see ADVERSE REACTIONS). This should be considered in the differential diagnosis of chest pain in a patient on therapy with pravastatin.

**Homozygous Familial Hypercholesterolemia:** Pravastatin has not been evaluated in patients with rare homozygous familial hypercholesterolemia. In this group of patients, it has been reported that HMG-CoA reductase inhibitors are less effective because the patients lack functional LDL receptors.

**Renal Insufficiency:** A single 20 mg oral dose of pravastatin was administered to 24 patients with varying degrees of renal impairment (as determined by creatinine clearance). No effect was observed on the pharmacokinetics of pravastatin or its 3 $\alpha$ -hydroxy isomeric metabolite (SQ 31,906). A small increase was seen in mean AUC values and half-life (t<sub>1/2</sub>) for the inactive enzymatic ring hydroxylation metabolite (SQ 31,945). Given this small sample size, the dosage administered, and the degree of individual variability, patients with renal impairment who are receiving pravastatin should be closely monitored.

**Information for Patients:** Patients should be advised to report promptly unexplained muscle pain, tenderness or weakness, particularly if accompanied by malaise or fever.

**Drug Interactions:** **Immunosuppressive Drugs, Gemfibrozil, Niacin (Nicotinic Acid), Erythromycin:** See WARNINGS: Skeletal Muscle.

**Anticypine:** Clearance by the cytochrome P450 system was unaltered by concomitant administration of pravastatin. Since pravastatin does not appear to induce hepatic drug-metabolizing enzymes, it is not expected that any significant interaction of pravastatin with other drugs (e.g., phenytoin, quinidine) metabolized by the cytochrome P450 system will occur.

**Cholestyramine/Colestipol:** Concomitant administration resulted in an approximately 40 to 50% decrease in the AUC of pravastatin. However, when pravastatin was administered 1 hour before or 4 hours after cholestyramine or 1 hour before colestipol and a standard meal, there was no clinically significant decrease in bioavailability or therapeutic effect. (See DOSAGE AND ADMINISTRATION: Concomitant Therapy.)

**Warfarin:** In a study involving 10 healthy male subjects given pravastatin and warfarin concomitantly for 6 days, bioavailability parameters at steady state for pravastatin (parent compound) were not altered. Pravastatin did not alter the plasma protein-binding of warfarin. Concomitant dosing did increase the AUC and C<sub>max</sub> of warfarin but did not produce any changes in its anticoagulant action (i.e., no increase was seen in mean prothrombin time after 6 days of concomitant therapy). However, bleeding and extreme prolongation of prothrombin time has been reported with another drug in this class. Patients receiving warfarin-type anticoagulants should have their prothrombin times closely monitored when pravastatin is initiated or the dosage of pravastatin is changed.

**Cimetidine:** The AUC<sub>0-12h</sub> for pravastatin when given with cimetidine was not significantly different from the AUC for pravastatin when given alone. A significant difference was observed between the AUC's for pravastatin when given with cimetidine compared to when administered with antacid.

**Digoxin:** In a crossover trial involving 18 healthy male subjects given pravastatin and digoxin concurrently for 9 days, the bioavailability parameters of digoxin were not affected. The AUC of pravastatin tended to increase, but the overall bioavailability of pravastatin plus its metabolites SQ 31,906 and SQ 31,945 was not altered.

**Gemfibrozil:** In a crossover study in 20 healthy male volunteers given concomitant single doses of pravastatin and gemfibrozil, there was a significant decrease in urinary excretion and protein binding of pravastatin. In addition, there was a significant increase in AUC, C<sub>max</sub>, and T<sub>max</sub> for the pravastatin metabolite SQ 31,906.

Combination therapy with pravastatin and gemfibrozil is generally not recommended.

In interaction studies with aspirin, antacids (1 hour prior to PRAVACHOL), cimetidine, nicotinic acid, or probucol, no statistically significant differences in bioavailability were seen when PRAVACHOL (pravastatin sodium) was administered.

**Other Drugs:** During clinical trials, no noticeable drug interactions were reported when PRAVACHOL was added to: diuretics, antihypertensives, digitalis, converting-enzyme inhibitors, calcium channel blockers, beta-blockers, or nitroglycerin.

**Endocrine Function:** HMG-CoA reductase inhibitors interfere with cholesterol synthesis and lower circulating cholesterol levels and, as such, might theoretically blunt adrenal or gonadal steroid hormone production. Results of clinical trials with pravastatin in males and post-menopausal females were inconsistent with regard to possible effects of the drug on basal steroid hormone levels. In a study of 21 males, the mean testosterone response to human chorionic gonadotropin was significantly reduced (p<0.004) after 16 weeks of treatment with 40 mg of pravastatin. However, the percentage of patients showing a  $\geq$ 50% rise in plasma testosterone after human chorionic gonadotropin stimulation did not change significantly after therapy in these patients. The effects of HMG-CoA reductase inhibitors on spermatogenesis and fertility have not been studied in adequate numbers of patients. The effects, if any, of pravastatin on the pituitary-gonadal axis in pre-menopausal females are unknown. Patients treated with pravastatin who display clinical evidence of endocrine dysfunction should be evaluated appropriately. Caution should also be exercised if an HMG-CoA reductase inhibitor or other agent used to lower cholesterol levels is administered to patients also receiving other drugs (e.g., ketoconazole, spironolactone, or metformin) that may diminish the levels or activity of steroid hormones.

**CNS Toxicity:** CNS vascular lesions, characterized by perivascular hemorrhage and edema and mononuclear cell infiltration of perivascular spaces, were seen in dogs treated with pravastatin at a dose of 25 mg/kg/day, a dose that produced a plasma drug level about 50 times higher than the mean drug level in humans taking 40 mg/day. Similar CNS vascular lesions have been observed with several other drugs in this class.

A chemically similar drug in this class produced optic nerve degeneration (Wallenian degeneration of retinogeniculate fibers) in clinically normal dogs in a dose-dependent fashion starting at 60 mg/kg/day, a dose that produced mean plasma drug levels about 30 times higher than the mean drug level in humans taking the highest recommended dose (as measured by total enzyme inhibitory activity). This same drug also produced vestibulocochlear Wallerian-like degeneration and retinal ganglion cell chromatolysis in dogs treated for 14 weeks at 180 mg/kg/day, a dose which resulted in a mean plasma drug level similar to that seen with the 60 mg/kg dose.

**Carcinogenesis, Mutagenesis, Impairment of Fertility:** In a 2-year study in rats fed pravastatin at doses of 10, 30, or 100 mg/kg body weight, there was an increased incidence of hepatocellular carcinomas in males at the highest dose (p<0.01). Although rats were given up to 125 times the human dose (HD) on a mg/kg body weight basis, their serum drug levels were only 6 to 10 times higher than those measured in humans given 40 mg pravastatin as measured by AUC.

The oral administration of 10, 30, or 100 mg/kg (producing plasma drug levels approximately 0.5 to 5.0 times human drug levels at 40 mg) of pravastatin to mice for 22 months resulted in a statistically significant increase in the incidence of malignant lymphomas in treated females when all treatment groups were pooled and compared to controls (p<0.05). The incidence was not dose-related and male mice were not affected.

A chemically similar drug in this class was administered to mice for 72 weeks at 25, 100, and 400 mg/kg body weight, which resulted in mean serum drug levels approximately 3, 15, and 33 times higher than the mean human serum drug concentration (as total inhibitory activity) after a 40 mg oral dose. Liver carcinomas were significantly increased in high-dose females and mid- and high-dose males, with a maximum incidence of 90 percent in males. The incidence of adenomas of the liver was significantly increased in mid- and high-dose females. Drug treatment also significantly increased the incidence of lung adenomas in mid- and high-dose males and females. Adenomas of the eye Harderian gland (a gland of the eye of rodents) were significantly higher in high-dose mice than in controls.

No evidence of mutagenicity was observed *in vitro*, with or without rat-liver metabolic activation, in the following studies: microbial mutagen tests, using mutant strains of *Salmonella typhimurium* or *Escherichia coli*; a forward mutation assay in L5178Y TK + / - mouse lymphoma cells; a chromosomal aberration test in hamster cells; and a gene conversion assay using *Saccharomyces cerevisiae*. In addition, there was no evidence of mutagenicity in either a dominant lethal test in mice or a micronucleus test in mice.

In a study in rats, with daily doses up to 500 mg/kg, pravastatin did not produce any adverse effects on fertility or general reproductive performance. However, in a study with another HMG-CoA reductase inhibitor, there was decreased fertility in male rats treated for 34 weeks at 25 mg/kg body weight, although this effect was not observed in a subsequent fertility study when this same dose was administered for 11 weeks (the entire cycle of spermatogenesis, including epididymal maturation). In rats treated with this same reductase inhibitor at 180 mg/kg/day, seminiferous tubule degeneration (necrosis and loss of spermatogenic epithelium) was observed. Although not seen with pravastatin, two similar drugs in this class caused drug-related testicular atrophy, decreased spermatogenesis, spermatocytic degeneration, and giant cell formation in dogs. The clinical significance of these findings is unclear.

**Pregnancy: Pregnancy Category X:** See CONTRAINDICATIONS.

Safety in pregnant women has not been established. Pravastatin was not teratogenic in rats at doses up to 1000 mg/kg daily or in rabbits at doses of up to 50 mg/kg daily. These doses resulted in 20x (rabbit) or 240x (rat) the human exposure based on surface area (mg/meter<sup>2</sup>). However, in studies with another HMG-CoA reductase inhibitor, skeletal malformations were observed in rats and mice. PRAVACHOL (pravastatin sodium) should be administered to women of child-bearing potential only when such patients are highly unlikely to conceive and have been informed of the potential hazards. If the woman becomes pregnant while taking PRAVACHOL (pravastatin sodium), it should be discontinued and the patient advised again as to the potential hazards to the fetus.

**Nursing Mothers:** A small amount of pravastatin is excreted in human breast milk. Because of the potential for serious adverse reactions in nursing infants, women taking PRAVACHOL should not nurse (see CONTRAINDICATIONS).

**Pediatric Use:** Safety and effectiveness in individuals less than 18 years old have not been established. Hence, treatment in patients less than 18 years old is not recommended at this time. (See also PRECAUTIONS: General.)

**ADVERSE REACTIONS**

Pravastatin is generally well tolerated; adverse reactions have usually been mild and transient. In 4-month long placebo-controlled trials, 1.7% of pravastatin-treated patients and 1.2% of placebo-treated patients were discontinued from treatment because of adverse experiences attributed to study drug therapy; this difference was not statistically significant. In long-term studies, the most common reasons for discontinuation were asymptomatic serum transaminase increases and mild, non-specific gastrointestinal complaints. During clinical trials the overall incidence of adverse events in the elderly was not different from the incidence observed in younger patients.

**Adverse Clinical Events:** All adverse clinical events (regardless of attribution) reported in more than 2% of pravastatin-treated patients in the placebo-controlled trials are identified in the table below, also shown are the percentages of patients in whom these medical events were believed to be related or possibly related to the drug.

Body System/Event	All Events %		Events Attributed to Study Drug %	
	Pravastatin (N=900)	Placebo (N=411)	Pravastatin (N=900)	Placebo (N=411)
Cardiovascular				
Cardiac Chest Pain	4.0	3.4	0.1	0.0
Dermatologic				
Rash	4.0*	1.1	1.3	0.9
Gastrointestinal				
Nausea/Vomiting	7.3	7.1	2.9	3.4
Diarrhea	6.2	5.6	2.0	1.9
Abdominal Pain	5.4	6.9	2.0	3.9
Constipation	4.0	7.1	2.4	5.1
Flatulence	3.3	3.6	2.7	3.4
Heartburn	2.9	1.9	2.0	0.7
General				
Fatigue	3.8	3.4	1.9	1.0
Chest Pain	3.7	1.9	0.3	0.2
Influenza	2.4*	0.7	0.0	0.0
Musculoskeletal				
Localized Pain	10.0	9.0	1.4	1.5
Myalgia	2.7	1.0	0.6	0.0
Nervous System				
Headache	6.2	3.9	1.7*	0.2
Dizziness	3.3	3.2	1.0	0.5
Renal/Genitourinary				
Urinary Abnormality	2.4	2.9	0.7	1.2
Respiratory				
Common Cold	7.0	6.3	0.0	0.0
Pharyngitis	4.0	4.1	0.1	0.0
Cough	2.6	1.7	0.1	0.0

\*Statistically significantly different from placebo.

The following effects have been reported with drugs in this class:

**Skeletal:** myopathy, rhabdomyolysis.

**Neurological:** dysfunction of certain cranial nerves (including alteration of taste, impairment of extra-ocular movement, facial paresis), tremor, vertigo, memory loss, paresthesia, peripheral neuropathy, peripheral nerve palsy.

**Hypersensitivity Reactions:** An apparent hypersensitivity syndrome has been reported rarely which has included one or more of the following features: anaphylaxis, angioedema, lupus erythematosus-like syndrome, polymyalgia rheumatica, vasculitis, purpura, thrombocytopenia, leukopenia, hemolytic anemia, positive ANA, ESR increase, arthritis, arthralgia, urticaria, asthenia, photosensitivity, fever, chills, flushing, malaise, dyspnea, toxic epidermal necrolysis, erythema multiforme, including Stevens-Johnson syndrome.

**Gastrointestinal:** pancreatitis, hepatitis, including chronic active hepatitis, cholestatic jaundice, fatty change in liver, and/or, rarely, cirrhosis, fulminant hepatic necrosis, and hepatoma, anorexia, vomiting.

**Reproductive:** gynecomastia, loss of libido, erectile dysfunction.

**Eye:** progression of cataracts (lens opacities), ophthalmoplegia.

**Laboratory Test Abnormalities:** Increases in serum transaminase (ALT, AST) values and CPK have been observed (see WARNINGS).

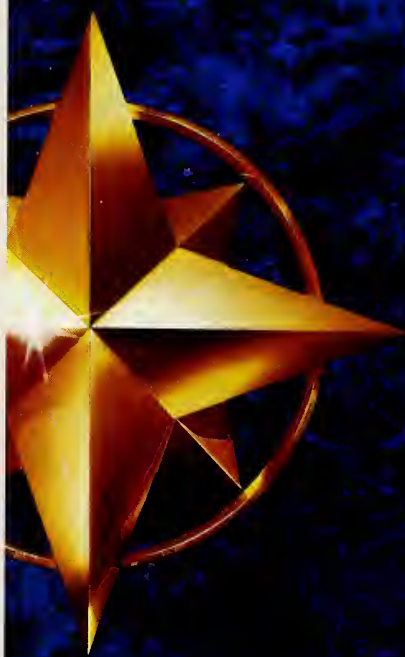
Transient, asymptomatic eosinophilia has been reported. Eosinophil counts usually returned to normal despite continued therapy. Anemia, thrombocytopenia, and leukopenia have been reported with other HMG-CoA reductase inhibitors.

**Concomitant Therapy:** Pravastatin has been administered concurrently with cholestyramine, colestipol, nicotinic acid, probucol and gemfibrozil. Preliminary data suggest that the addition of either probucol or gemfibrozil to therapy with lovastatin or pravastatin is not associated with greater reduction in LDL cholesterol than that achieved with lovastatin or pravastatin alone. No adverse reactions unique to the combination or in addition to those previously reported for each drug alone have been reported. Myopathy and rhabdomyolysis (with or without acute renal failure) have been reported when another HMG-CoA reductase inhibitor was used in combination with immunosuppressive drugs, gemfibrozil, erythromycin, or lipid-lowering doses of nicotinic acid. Concomitant therapy with HMG-CoA reductase inhibitors and these agents is generally not recommended (See WARNINGS: Skeletal Muscle and PRECAUTIONS: Drug Interactions).

**OVERDOSAGE**

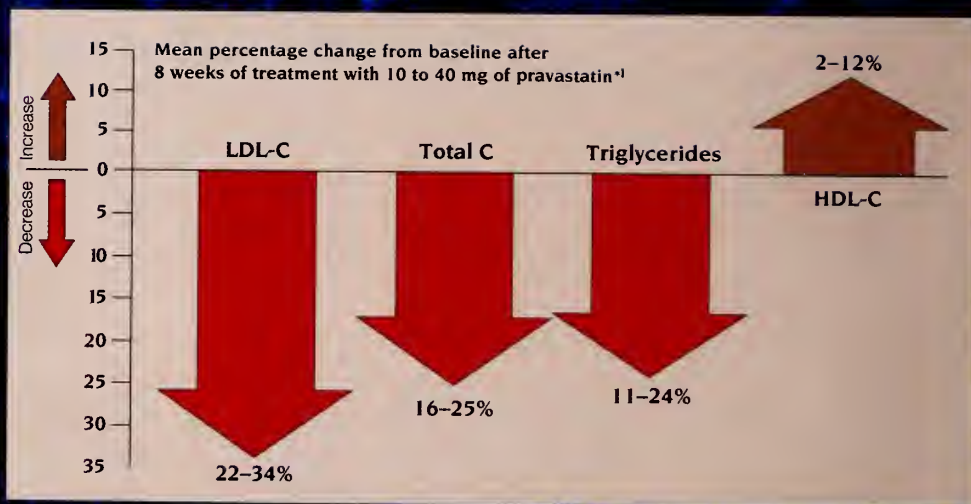
There have been no reports of overdoses with pravastatin. Should an accidental overdose occur, treat symptomatically and institute supportive measures as required.





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<sup>\*1</sup>Each arrow represents a range of means derived from a single placebo-controlled study that included 55 patients treated with pravastatin.

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**Reference:** 1. Jones PH, et al. Once-daily pravastatin in patients with primary hypercholesterolemia: a dose-response study. *Clin Cardiol.* 1991;14:146-151.

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Please see CONTRAINDICATIONS, WARNINGS, PRECAUTIONS, and ADVERSE REACTIONS in the brief summary of prescribing information on the adjacent page.



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## MATERNAL MORTALITY



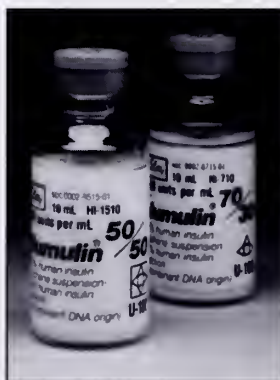




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FEBRUARY 1993

VOLUME XXXIV

NUMBER 2

## SCIENTIFIC ARTICLES

- Maternal Mortality In Mississippi: 1987-1991** 35  
*James L. Moore, Jr, MD; Suneet P. Chauhan, MD;  
William B. Wiener, MD and John C. Morrison, MD*
- Unsuspected Arterial Injury** 42  
*Michael H. Bross, MD and Anne Stefani, MD*

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## SPECIAL ARTICLE

- Mississippi State Board of Medical Licensure** 46  
**Annual Report July 1, 1991 Through June 30, 1992**  
*Frank J. Morgan, Jr., MD*

## EDITORIALS

- Reform, Resolve and Reaffirmation** 54  
*William C. Gates, Jr., MD*
- Letter to God** 56  
*Joseph E. Johnston, MD, Associate Editor*

## DEPARTMENTS

- Medical Organization** 59
- From the University of Mississippi Medical Center** 62
- New Members** 64
- Deaths** 66
- Personals** 67
- Placement Service** 70

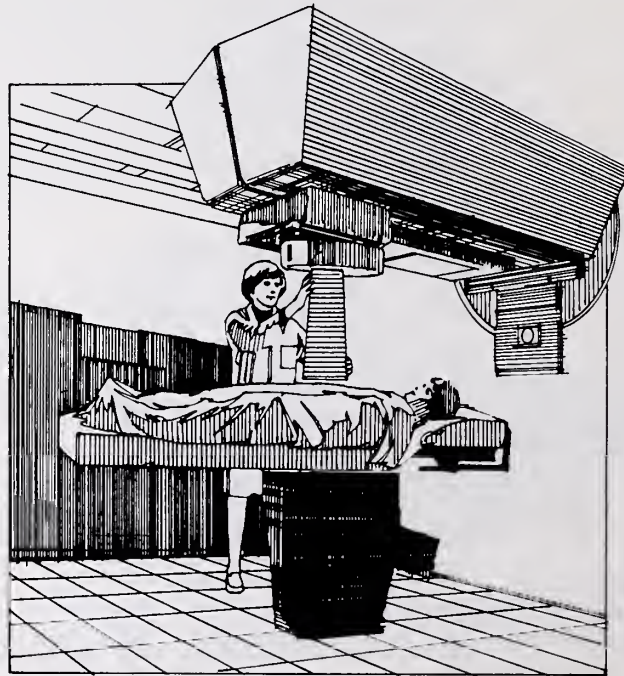
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Journal of the Mississippi State Medical Association  
Volume XXXIV, Number 2

## 125th Annual Session Scientific Exhibits

The MSMA 125th Annual Session will be held April 28 - May 2, 1993 at the Royal d'Tberville Hotel, Biloxi. Physicians who would like to reserve **Scientific Exhibit Space** should write: **Scientific Exhibits, MSMA, PO Box 5229, Jackson, MS 39296-5229** or FAX this information to (601) 352-4834. The letter requesting exhibit space should include the following information:

- (1) **the title of the exhibit;**
- (2) **the author(s) of the exhibit;**
- (3) **an estimate of the amount of exhibit space needed (MSMA will provide a table - all other materials are to be supplied by the exhibitor);**  
**and**
- (4) **a brief synopsis of the subject to be exhibited.**

\*\*\*

## MS Ranks 6th In Disciplining Physicians

Jackson, MS - Mississippi continues to rank at or near the nation's top in disciplining negligent and careless physicians, a national consumer group said.

Mississippi which lend the nation in disciplining physicians in 1989, ranked sixth in a report released by Public Citizen at a Washington news conference.

"The Mississippi State Board of Medical Licensure has been one of the most active a boards in the country," the group said.

The state took disciplinary actions against 53 of the state's 3,753 licensed physicians, and 34 of those were considered serious. Those physicians lost their licenses or were placed on probation.

Mississippi punished 66 in 1989 and has ranked in or near the top 10 since 1988, Public Citizen said.

"We're very pleased over that. The members of this board take their jobs very seriously," said Dr. Frank Morgan, the board's executive director.

Public Citizen said Mississippi's reporting laws are too lax. It recommended that Legislature loosen the board's ties to the Mississippi Medical Association, which nominates the board's nine physician-members, and allow the governor to appoint someone. At least three should be non-physician, public members, Public Citizen said.

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## **Pro Updates Set For March**

Changes in the peer review process will be discussed at three regional workshops scheduled in March by the Mississippi Foundation for Medical Care (MFMC), the federally designated peer review organization (PRO) for the state.

The PRO Update sessions will feature reports from Dr. James S. McIlwain, MFMC medical director, and Dr. Alton B. Cobb, principal clinical coordinator.

The workshops will be March 9 at Northwest Community College Coliseum in Senatobia; March 11 at Ramada Inn Metro, Jackson; March 31 at Holiday Inn Airport in Gulfport.

Interested person should contact the MFMC Communications Department at 354-0304 for further information.

\*\*\*

## **Nation's Top Disability Administrator Takes Mississippi Job**

Jackson, MS - Nell C. Carney, who has headed the nation's agency for disabled American since July 1989, has accepted the helm of the state's Department of Rehabilitation Services. "It is my full intention to make the rehabilitation program in Mississippi a national model," Carney said in an interview from her Washington office.

Ms. Carney, 47, replaces John Cook as executive director of an agency that serves more than 100,000 Mississippians. Cook left the \$73,258-a-year position in December. Ms. Carney, who is visually impaired, begins work in January.

She holds a master's degree from Vanderbilt University and more than 90 hours of additional management training at the University of Washington, the Wharton School of Business at the University of Pennsylvania, Virginia Commonwealth University and the University of Oklahoma.

\*\*\*

## **Surgeon Develops Helmet To Reduce Injuries**

Meridian, MS - Word is getting out on the RushAir SpineSaver. Meridian orthopaedic surgeon Dr. Gus "Sonny" Rush will address a group of the National Football League's strength and training coaches in Indianapolis, Feb. 18-19, regarding his development of a football helmet with an air bag. A spokesman for NFL fitness personnel called and invited Dr. Rush to the meeting after seeing a story in the New Orleans *Times Picayune*.

"It's just incredible how word is getting out," said Dr. Rush. "The technology has not been here," he said. "Basically we're still looking at the future, but I really believe this thing will work." The helmet which includes an air bag, similar to air bags in automobiles, that would deploy when a certain amount of pressure is applied to the top of the helmet should be ready for testing in one to two years.

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# Maternal Mortality In Mississippi: 1987-1991

JAMES L. MOORE, JR. MD  
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WILLIAM B. WIENER, MD  
JOHN C. MORRISON, MD

Beginning in 1957, a committee was established by the Mississippi State Medical Association (MSMA) with the purpose of reducing maternal mortality within the state. The objective of this committee is to analyze all cases involving a maternal mortality in order to prevent future deaths associated with pregnancy through education of clinicians in Mississippi. The emphasis of the overall study is directed at improvement of maternal care, and this effort has enjoyed the support of practitioners throughout the state. The maternal mortality rate in our state, expressed as maternal deaths per 100,000 live births, was 90.2 from 1957-1966, 42.4 from 1967-1986, 11.8 from 1977-1976, and 14.1 from 1987-1991. The maternal mortality rate for the United States was 35.5, 19.0, 9.3, and 7.6 for the same time periods. Figure 1 compares the maternal mortality for the nation and our state

**OBJECTIVE:** To characterize the maternal mortality in the state of Mississippi for 1987-1991 and compare the maternal mortality from 1977-1986 with that of the last 5 years.

**STUDY DESIGN:** Factors associated with maternal mortality were obtained from death certificates, replies to questionnaires, medical records, and autopsy reports.

**RESULTS:** The maternal mortality rate in Mississippi for 1987-1991 (14.1/100,000) was not significantly different than for 1977-1986 (11.8/1000,000;  $P = 0.45$ ). Over the last 5 years there was an increased incidence of direct obstetric deaths (50% vs 73%). During 1987-1991, toxemia as a cause of death for parturients decreased, while hemorage as a cause of maternal death increased. There was a rise in the incidence of patient related factors which were avoidable and which led to several deaths during 1987-1991.

**CONCLUSION:** The state's maternal mortality rate remains stable. Improved patient and health care provider's education are necessary to further decrease the incidence of maternal death in Mississippi.

during this period (1957-1991). The graph illustrates a dramatic decline in maternal death in Mississippi as well as the nation over the last 34 years.

In 1964, the American Medical Association (AMA) pub-

lished guidelines for the study of maternal deaths.<sup>1</sup> The Committee on Maternal and Child Care for Mississippi, using the AMA format, has recently completed a review of the data for the calendar years 1987-1991,

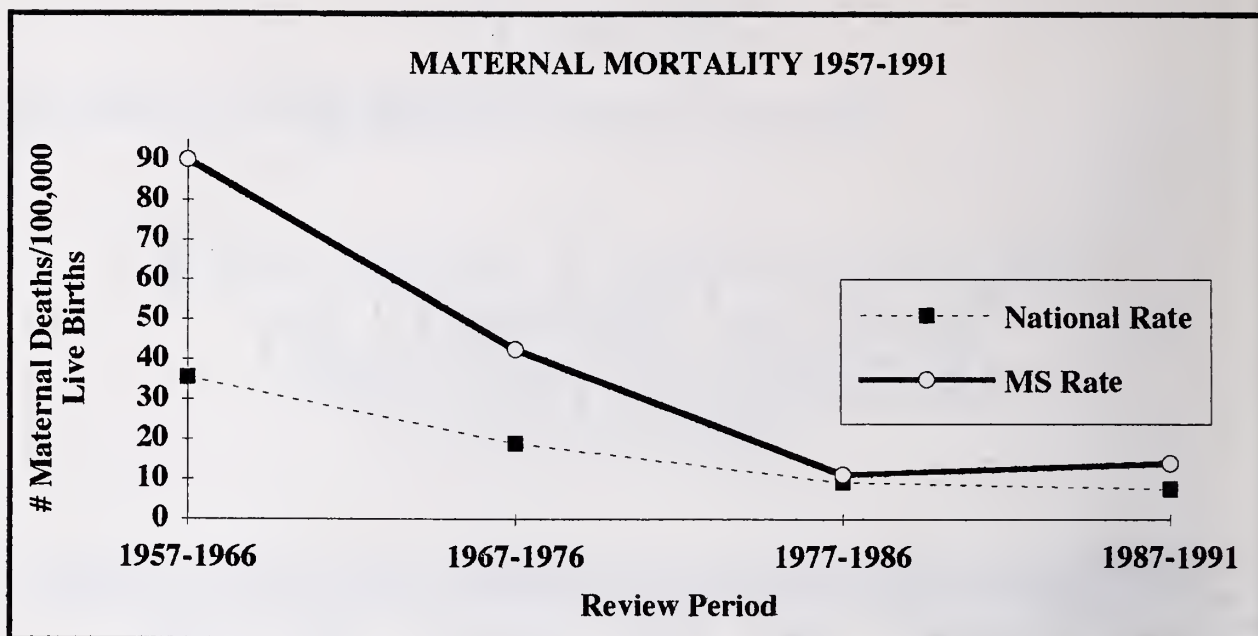


Figure 1

the results of which are presented here.

## METHODS

The operational protocol for the Committee on Maternal and Child Care has served the state well over the past 35 years of study. A questionnaire type of inquiry has been exclusively used. No investigations of hospital or office records have been undertaken nor have interviews of physicians been conducted. Complete anonymity is guaranteed and the records of the deliberation as well as the facts surrounding each case are free from litigious activities.

Using death certificate data, all maternal deaths during gestation or within six months of delivery are referred to the Committee on Maternal and Child Care by the Department of Vital Statistics for the State Department of Public Health following a birth/death certificate match. A letter from the committee chairman is sent to the

physician who attended the patient during the course of her pregnancy and/or delivery. A data sheet is also forwarded to the physician to assist in retrieval of pertinent information. In addition, a short descriptive report is also requested from the physician. Postmortem examinations are strongly encouraged and a copy of the final autopsy report is requested in this initial letter. Follow-up letters are sent at appropriate intervals if the committee receives no reply. Information may also be gathered by the health department. Personal contacts by the committee are occasionally used to obtain this information. Additionally, letters requesting more information may be sent to the attending physician if supplemental data might provide clinically useful data.

Following receipt of the completed data sheet, the autopsy report, the descriptive summary, and any other pertinent information, all identifying

marks are removed by the MSMA in such a way that complete anonymity for both the attending physician and the hospital or clinic is preserved. A copy of the case information is then forwarded to a member of the Committee on Maternal and Child Care. The case is then reviewed by the committee member in accordance with the American Medical Association's *Guide For Maternal Death Studies*.<sup>1</sup> At a meeting of the committee, this member presents a summary of that particular case. The case is then openly discussed by the committee, with complete respect for anonymity. After discussion, the case is classified according to the AMA guidelines as discussed below. The findings of the committee are then furnished to the attending physician, but are otherwise not released. The AMA guidelines for maternal mortality case review allows a standard classification for each maternal death investigation. By



following this protocol, each maternal mortality is classified with respect to adequacy of data collection, cause of the death, and avoidability of the demise.

Upon initial discussion of information by the committee, the data is evaluated as to its utility. Those cases that have sufficient data are further classified according to the adequacy of the furnished information. The adequacy rating uses a five-point scale, with the highest rating (5) reserved for those cases in which all three investigative criteria are fulfilled. These three criteria include completion of the questionnaire for data collection, submission of a relevant note or clinical explanation, and formal autopsy report. A rating of 4 occurs when the autopsy is not performed but the other two criteria are met. If only the data questionnaire is filled out, a rating of 3 is assigned, but if the data sheet is incompletely filled out the rank is reduced to 2. A level of 1 is assigned to cases in which a reply is received from the attending physician, but none of the three criteria is fulfilled. Cases with an adequacy rating of 1 or 2 are very difficult to objectively evaluate because of significant gaps in the data. It is in these cases that personal follow-up by a committee member is helpful in obtaining data for review. In addition, assistance from the State Department of Health and from the particular hospitals involved through the State Hospital Association has proven invaluable in difficult cases.

After a review of the case by the committee, the maternal death is classified as resulting from direct obstetric causes, indirect obstetric causes, or unde-

termined causes. Direct obstetric deaths are defined as those in which the principal cause of death is a condition directly related to pregnancy. Examples of this include postpartum hemorrhage, antenatal hemorrhage, preeclampsia/eclampsia, infection, vascular accidents, and deaths related to anesthetic complications. Indirect obstetric deaths are those resulting from a disease that was present prior to conception, or developed during the gestation but was not aggravated by the physiologic changes associated with pregnancy. Examples of this include deaths due to diabetes, cardiac disease, and pulmonary disease.

The final analysis of each case concerns its avoidability. A case is avoidable if, under ideal circumstances (the attending physician possesses all the currently available knowledge concerning the factors related to the cause of death, has a high level of technical competence and has the services of a well organized and properly equipped hospital), the demise would not have occurred. All direct obstetric deaths are evaluated as to avoidability, and those cases judged to be avoidable are further scrutinized to determine whether the avoidability is due to professional, hospital, or patient factors.

RESULTS

The results of the maternal mortality review for the calendar years 1987-1991 by the Committee on Maternal and Child Care are summarized in Tables I-III. For these five years, there were 30 maternal deaths among 213,076 live births, yielding a maternal mortality rate of 14.1 per 100,000 live births (Table I). During 1987-1991, there appeared to be a slight increase in maternal mortality, however, the rate was not significantly different from 1981-1986 ( $P=0.45$ ). Interestingly, 20 of these deaths (67%) occurred in two calendar years. When these two years are excluded from review, the maternal mortality rate is 7.9%. This is equal to the national average and markedly lower than ever recorded for the state of Mississippi.

The committee is pleased to report that replies were received concerning each of the 30 maternal death investigations, and 97% of the replies contained appropriate information that was judged by the committee to be usable (Table II). However, it is disturbing that formal autopsies were obtained in fewer than one-third of the maternal deaths (Table III). Additionally, it remains a concern that nearly 20% of the committee inquiries yielded suboptimal information

Table 1 - MATERNAL MORTALITY 1957-1991		
Review Period	National Rate	Mississippi Rate
1957-1966	35.5	90.2
1967-1976	19.0	42.4
1977-1986	9.3	11.8
1987-1991	7.6	14.1
Number of maternal deaths per 100,000 live births		

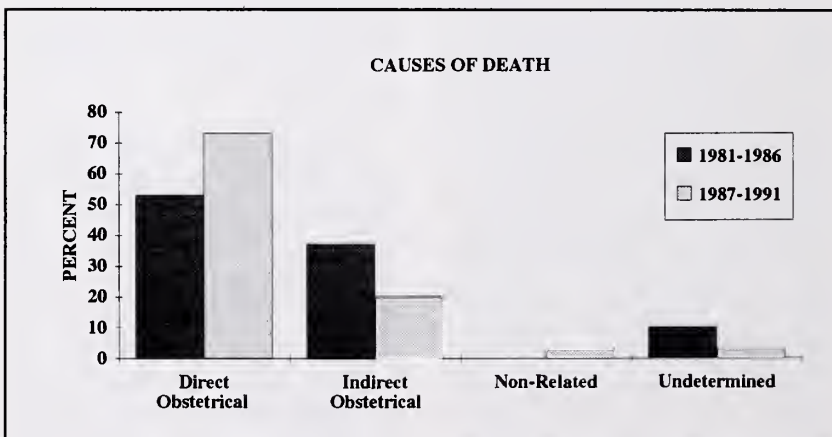


**Table 11 - STUDY MATERIAL  
1987-1991**

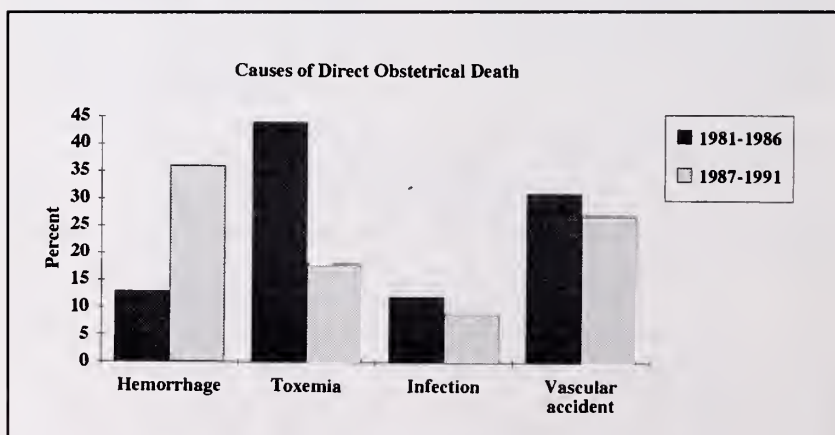
	Number	Percent
Total Cases	30	-
Replies Received	30	100
Usable Data	29	97

**Table III - ADEQUACY OF DATA**

Category	Number	Percent
5	8	27
4	15	50
3	2	7
2	3	10
1	2	7



**Figure 2**



**Figure 3**

as defined by category 1 and 2. The need for complete information is obvious if we are to carry out our educational goal and prevent maternal mortality.

## DISCUSSION

The percentage of maternal deaths attributable to direct obstetric causes is higher for this review period than in previous years.<sup>2</sup> During 1981-1986, approximately 50% of the deaths were due to direct obstetric causes, while this figure approaches 75% for the current review period (Figure 2). Other authors have found a decreasing proportion of direct obstetric deaths in other sections of the United States.<sup>3,4</sup> With respect to particular obstetric complications linked to maternal deaths, Figure 3 compares the relative frequency regarding the causes of maternal deaths during 1981-1986 and 1987-1991. Although hypertension has been reduced by over 50%, deaths from hemorrhage have increased by three-fold. The fact that preeclampsia/eclampsia is less frequently associated with maternal deaths during the past five years likely reflects the heightened awareness among clinicians in the state concerning this disease. Obstetric hemorrhage sufficient to cause maternal death was not frequently due to delay in patients seeking health care, thus, emphasizing the need for patient education to prevent maternal morbidity.

There has been no appreciable change in the statistics with respect to avoidability during the two periods (1981-1986 and 1987-1991). Approximately 50% of the deaths were deemed avoidable according to the

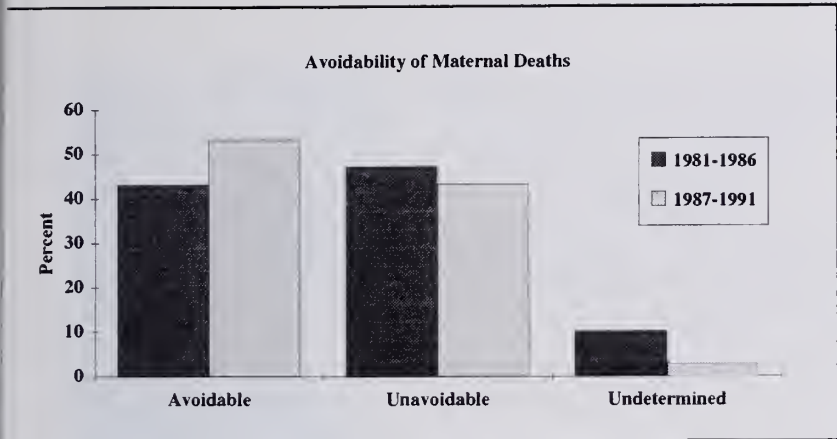


Figure 4

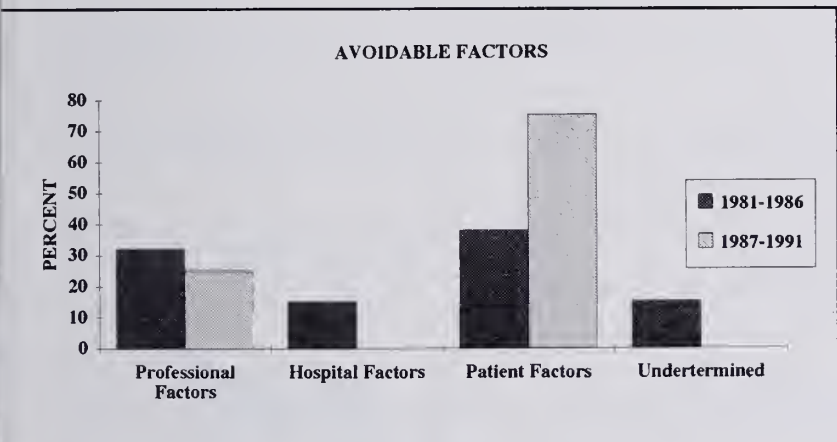


Figure 5

AMA guidelines (Figure 4). As depicted in Figure 5, the overwhelming majority of avoidability factors center upon acts of omission by the patients themselves. Patient education is critically important to reduce the maternal mortality rate. Perhaps five years from now, when the next maternal mortality review is published, we will observe a dramatic reduction in maternal deaths because of more funding for patient education and better prenatal care.

In conclusion, there are several important concepts to be gained from this review. All physicians practicing obstetrics should appreciate that absolute

anonymity is the rule throughout this assessment by the Committee on Maternal and Child Care. The clinician should feel comfortable sharing all pertinent information so that an accurate appraisal of the maternal death is accomplished via the goal of education. As physician education has reduced hypertension and anesthesia related deaths, with early patient education the incidence of obstetric hemorrhage as the cause of death should also decrease. We must remember that an informed patient, who realizes the danger signs of impending complications, is our goal. For as long as there are maternal deaths to re-

port, we should continue to refine our thrust toward provider and patient education. □

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# Unsuspected Arterial Injury

MICHAEL H. BROSS, MD  
ANNE STEFANI, MD

**A**lthough arterial injuries are often suspected with penetrating injuries, the effects of blunt trauma may be missed. Serious iliac artery injuries have been reported from relatively minor trauma, with delayed onset of symptoms and diagnosis.<sup>1</sup> A missed diagnosis can have devastating effects, with unacceptably high amputation rates.<sup>2</sup> This case describes a serious arterial injury from bicycle-related trauma.

## CASE REPORT

A six year old boy was brought to the emergency department after falling from his bicycle. During the fall, the handlebar struck his right groin area. He complained immediately to his mother of groin pain. Although the boy had complained of leg pain on prior occasions with negative medical findings, this episode was un-relieved by conservative measures at home and prompted an emergency department visit.

On arrival at the emergency department, the boy was in no acute distress. He denied any pain at rest. Vital signs revealed a temperature of 99.6 Fahrenheit, pulse of 100, respirations

24, blood pressure 106/70, and weight 45 pounds. Physical examination of the head, neck, chest, back, and genitalia were unremarkable. The abdomen was scaphoid without contusion. Normal bowel sounds were auscultated. There was significant tenderness to palpation above the right inguinal ligament. Extremity examination revealed tenderness at the right femoral area, without swelling or contusion. Leg pulses were noted to be +3 on the left (femoral, popliteal, dorsalis pedis, posterior tibial). Leg pulses on the right were +1 femoral and not palpable below the femoral artery. The right leg was warm with good capillary refill. Leg blood pressures, using a Doppler device at the popliteal artery, were 110 mm Hg left and 60 mm Hg right. Upon walking, he avoided placing any weight on his left heel, complaining of a splinter injury ten days ago. There was a small puncture wound with purulent drainage from the left heel. The child had no pain or limp from his injured right groin area. Neurological examination was unremarkable.

Initial laboratory findings included normal electrolytes,

blood urea nitrogen, creatinine, calcium, and glucose. Complete blood count revealed a hemoglobin of 10.0 g/dl and a white blood cell count of 10,600. Clotting studies were within normal limits. Urinalysis revealed specific gravity of 1.025, pH 5.0, negative dipstick tests, negative bacteria, 20-25 white blood cells, and no red blood cells.

Initial X-ray findings included negative flat and upright abdomen, right hip, and left foot studies.

With physical findings suggestive of arterial injury, surgery and radiology consultations were obtained. The radiologist recommended initial CT examination of the abdomen and pelvis. There was no evidence of extravasation or gross obstruction of the right femoral artery. The liver, spleen, aorta, and mesenteric vessels appeared normal. A follow-up film showed good renal function with no abnormality of the calices, ureters, or bladder.

The patient was admitted to the intensive care unit for close observation. Examination on the following day revealed a continued pulse deficit in the right leg. Systolic blood pressure in

he right popliteal area rose to 90 mm Hg. Doppler examination by the surgical consultant revealed biphasic right iliac and femoral signals suggestive of arterial injury. An arteriogram showed occlusion of the right external iliac artery approximately 1 cm from its origin, with no contrast seen in the right common femoral artery. Reconstitution was demonstrated, with delayed blood flow, at the level of the origin of the profunda femoral and superficial femoral arteries. The procedure was well tolerated.

Abdominal laparotomy and exploration of right groin were performed the next morning. At the inguinal ligament, there was a contused 3/4 cm area of external iliac artery with disruption of the arterial intima, clot formation, and obstruction. The contused area was resected and an end-to-end anastomosis was performed. There was good blood flow, and distal pulses were restored.

The patient did well after the surgery, with no fever or complications. Leg pulses remained intact. On the sixth post-op day, a one cm wood splinter was removed from the left heel. Follow-up urinalysis and culture were negative. Patient was discharged on the seventh post-op day, ambulating well.

## DISCUSSION

Although this child presented with a serious injury, there were multiple confusing factors. He was limping from a splinter injury to the opposite foot, had a history of previous leg pains, and denied pain from the acute injury. A good physical examination revealed absent pulses and a lower blood pressure in the in-

jured leg. With immediate suspicion of arterial injury, appropriate consultations were made. The best physical examination predictors of lower-extremity arterial injury have been reported to be pulse deficit and delayed capillary refill.<sup>3</sup> Blood pressure measurements which are 10 to 20 mm Hg lower in the injured leg indicated a need for arteriography.<sup>2</sup> The normal triphasic Doppler signal will be altered with a significant proximal occlusive lesion.<sup>2</sup> CT scanning in children is compromised by limited cooperation and a lack of retroperitoneal fat.<sup>4</sup> As noted in this case, CT scanning of vascular structures has limitations and may miss the diagnosis. The test of choice for suspected arterial injury is the arteriogram.<sup>5,6</sup> Arteriograms, selectively performed for abnormal clinical findings, will identify significant arterial injuries.<sup>3</sup>

The ratio of blunt to penetrating trauma is much higher in children than adults. Childhood trauma results in force applied over a smaller area, with less skeletal mass to protect underlying structures. Internal organ damage is more likely to occur.<sup>4,7</sup> Trauma from bicycle handle bars has resulted in a wide variety of abdominal and genital injuries.<sup>8-10</sup> As illustrated by this case, the iliac vessels are prone to injury as they leave the bony pelvis.<sup>1</sup>

Bicycles need to be recognized as potential causes of serious injury. Young bicycle riders can attain high speeds and often lack good judgement. As physicians, we need to promote safe bicycle riding and helmet protection. □

2500 North State Street  
Jackson, Mississippi

## ACKNOWLEDGEMENTS

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# Mississippi State Board Of Medical Licensure Annual Report July 1, 1991 through June 30, 1992

**FRANK J. MORGAN, JR., MD  
EXECUTIVE OFFICER**

**T**he Mississippi State Board of Medical Licensure is the State's legally constituted Licensure Board for physicians (MD), osteopathic physicians (DO), and podiatrists (DPM). The Board, which meets bimonthly on the third Thursday beginning in January of each year, is composed of nine physicians appointed to staggered terms by the Governor.

The Board is responsible for setting policies and professional standards concerning the practice of physicians (MD), osteopathic physicians (DO), and podiatrists (DPM); considering applications for licensure; conducting examinations for licensure; investigating legitimate drug traffic among medical practitioners under the Uniform Controlled Substances Act; conducting investigations in disciplinary matters involving violations

of state and federal laws; probation, suspension and revocation of licenses; considering petitions for terminations of probationary and suspension periods and restoration of revoked licenses; promulgating reasonable rules and regulations necessary to enable it to discharge its functions; and enforcing the provisions of the law regulating the practice of medicine.

The administrative functions of the Board are performed under the direction of its Executive Officer, Frank J. Morgan, Jr., MD, by eleven full-time staff members, including five investigators; an administrative assistant; a licensing officer; an accountant, and two secretaries. The office of the Board is located at 2688-D Insurance Center Drive, Jackson, Mississippi 39216.

### Licensure

Any physician, osteopathic physician, or podiatrist desiring to practice medicine in Mississippi must first obtain a license to do so by contacting the Board. When an inquiry concerning licensure is received, a questionnaire to elicit certain pertinent information is sent to the practitioner, a determination is made as to his eligibility for licensure. Names of references submitted on the questionnaire, as well as the American Medical, Osteopathic, or Podiatric Medical Associations; other states in which the practitioner has held staff privileges are sent inquiries. If the information received is favorable, an application is sent to the physician.

### Reciprocity/Endorsement

The Board of Medical Licensure may grant licenses to practice medicine without examina-



on as to learning, to graduates in medicine, osteopathic medicine, or podiatry who hold licenses to practice from other states, provided the requirements in such states are equal to those set forth by the Mississippi Board. In addition, this Board may affiliate with and recognize for the purpose of waiving examination, diplomates of the National Board of Medical Examiners, the National Board of Osteopathic Medical Examiners and the national Board of Podiatry Examiners in granting licenses to practice in Mississippi.

During FY92, **939** practitioners requested applications for licensure by reciprocity with other states or through endorsement of the examinations given by the National Board of Medical, Osteopathic, and Podiatric Examiners. Based upon these requests, **330** applications were processed and approximately **11,780** reference inquiries were made by the Office of Medical Licensure to determine the eligibility of applicants for a license to practice in Mississippi.

Following receipt of favorable certificates of training and personal interviews, a total of **354** physicians, **10** osteopathic physicians and **5** podiatrists were licensed in Mississippi.

In addition, **4** temporary medical licenses which allowed applicants 30 days in which to complete the necessary requirements for permanent licensure were issued.

Effective July 1, 1982, an amendment to the Medical Practice Act permitted the issuance of temporary licenses to non-resident and retired resident physicians to practice for up to 90 days in *licensed youth camps* in Mississippi. **Five (5)** such li-

censes were issued during FY92.

### Examination

The nationally administered Federation Licensing Examination (FLEX) was adopted as the state's medical licensing examination in 1973. The three-day FLEX is a written objective-type, comprehensive examination which tests applicants in the basic sciences, clinical sciences, and clinical competence. Component I is designed to evaluate measurable aspects of knowledge and understanding of basic and clinical science. Component II focuses on critical abilities and knowledge required for diagnosis and management of selected ambulatory and inpatient clinical problems representing a core of clinical situations frequently encountered by the physician licensed for the independent practice of medicine. A score of 75 is required on each component for passing. The FLEX is given in June and December of each year, and the dates are set by the FLEX Board of The Federation of State Medical Boards of the United States, of which this Board is a member.

Applicants for licensure by examination are screened in the same way as those seeking licensure by reciprocity. References are obtained and credentials are checked thoroughly. During FY92, **103** applicants were declared eligible and took the examination. **Ninety-eight** passed both components. Those applicants who were successful will be granted licensure upon their submitting documentation of completion of one year of accredited postgraduate training.

Beginning in the Spring of

1988, SPEX (Special Purpose Examination) was offered as a quarterly administration: March, June, September, and December. The June and December SPEX administrations are set to coincide with the last day of the three-day FLEX administration.

This one-day examination is administered to applicants who possess all the qualifications for licensure by reciprocity/endorsement, with the exception of having successfully passed a written medical competency examination within a 10-year period prior to filing his/her application.

In FY92, **13** candidates made application and took SPEX. **Five** failed and **eight** passed.

A total of **61** restricted temporary licenses were issued for the period July 1, 1991 through June 30, 1992, to applicants for licensure who entered their first year of postgraduate training at the University of Mississippi Medical Center, Jackson. The temporary licenses permitted them to practice only within the scope of their respective residency training programs at the University.

### Limited Institutional Licensure

In addition to licensure by examination and reciprocity, state law also provides for limited institutional licensure which is available only to graduates of foreign medical schools for their employment in state-supported institutions. It was the intent of the law to enable Mississippi institutions to utilize the services of qualified foreign medical graduates during the period necessary for them to meet the requirements for permanent licensure.

Based upon their presenting to the Office of Medical Licensure their original medical diplomas, documentation of certificates from the Educational Commission for Foreign Medical Graduates (ECFMG), Visa Qualifying Examination (VQE), or Foreign Medical Graduate Examination in the Medical Sciences (FMGEMS), and favorable references, **12** applicants were issued limited institutional licenses to practice in state-supported institutions. In addition, **25** limited institutional licenses were renewed during this period.

Since limited institutional licensure was established in 1971, **369** such licenses have been issued. As of June 30, 1992, a total of **5** of the limited institutional licensees have met all requirements, including passing the FLEX and fulfilling the post-graduate training requirements, and have been issued permanent medical licenses in Mississippi.

### **Certification and Verification**

A practitioner originally licensed in Mississippi by examination who seeks licensure in another state through reciprocity must have his license in this State and the scores he obtained on the licensure examination certified by this Board to the reciprocating state. **398** such certifications were made by the Office of Medical Licensure during FY92 and **142** letters of good standing were completed.

The Board also verified the licensure status of practitioners to health care providers, health insurance carriers, licensing board of other states, and state and federal law enforcement and regulatory agencies. Approximately **6,462** verifications of licensure were made by this

Board during FY92.

### **Annual Renewal**

The license of every physician, osteopathic physician, and podiatrist licensed to practice in the state must be renewed annually. On or before May 1, of each year, an application for renewal of license is mailed to all practitioners licensed by this Board to practice in Mississippi. The application must be completed and returned to the Board along with the renewal fee by June 30.

Based upon information given on the renewal applications, as of July 1, 1991, there were **5,909** physicians licensed to practice medicine in Mississippi. Of this number **3,634** resided and practiced in state, and **2,275** resided out of state.

A total of **1,618** in-state physicians worked in the primary care specialties, which include family practice, **526**; general practice, **209**; internal medicine, **433**; pediatrics, **228**; and obstetrics and gynecology, **222**.

As of July 1, 1992, **6,105** practitioners had renewed for the period July 1, 1992 through June 30, 1993. **3,687** practice and reside in Mississippi and **2,418** reside out of state, but elected to maintain current licensure in Mississippi.

### **Investigations**

Under the direction of the Executive Officer, the Board's five investigators carried out the responsibilities of investigating alleged violations of the Medical Practice act and the Mississippi Uniform Controlled Substances Act as it applies to medical practitioners. During the fiscal year the Board received **280** complaints regarding alleged

violations from various sources including state and federal law enforcement officials, state and federal regulatory agencies, hospital administrators, local and state medical societies, medical licensing boards of other states, health professionals, and lay individuals. A total of **180** practitioners or individuals were investigated by the Medical Board investigative staff. In conducting these investigations and inspections a total of **953** pharmacies were profiled throughout the State of Mississippi. Analysis of the **180** investigations revealed **117** practitioners were investigated for suspicious or excessive prescribing of controlled substances; **2** involved personal abuse of alcohol; **16** involved failing to keep records of substances dispensed/prescribed; **7** involved personal use of or addiction to drugs; **1** involved mental illness; **19** investigations involved unprofessional conduct; **10** involved the illegal practice of medicine; **2** involved sexual abuse of patients; **6** follow-up compliance investigations were made. Of the **117** investigations involving suspicious or excessive prescribing patterns, **57** of these practitioners were written letters by the Executive Officer warning them against future violation of federal and state laws regarding prescribing of controlled substances. Additionally, **72** urine screens were collected and **16** audits of drugs handled by dispensing physicians were accomplished.

As a result of the investigations **9** practitioners had their privileges (DEA Certificate) authorizing them to handle controlled substances restricted. **Seven (7)** of these investigations



involved physicians who were personally abusing controlled substances, and 2 involved excessive prescribing.

**Disciplinary Actions**

Additionally, investigations conducted by the Board resulted in 11 disciplinary hearings. Following consideration of these matters, 6 licenses were revoked; 1 medical license by reciprocity was denied; 1 license was revoked, revocations stayed and license placed on probation; 1 license suspended, suspension stayed until certain conditions were met; 1 licensee ordered not to practice until license in another state was cleared.

Petitions for removal of restrictions were considered on 6 medical license. Of these, the Board denied 3 and granted 3.

Six (6) physicians requested reinstatement of their medical licenses. Four (4) were denied and 2 were granted.

In another actions, the Board granted 11 licenses by reciprocity and denied 6. One (1) request for waiver on limited institutional license was granted, 1 request to change practice location was granted, and 1 voluntary surrender of medical license was accepted.

Twelve (12) physicians had their controlled substances prescribing privileges restores and 1 physician was denied permission to re-register with the Drug Enforcement Administration for prescribing privileges.

Entering into Consent Agreements with 13 physicians, the Board revoked 1 license, stayed the revocation and placed license on probation; suspended 3 licenses, stayed the suspensions and placed licenses on probation; suspended 1 license; ac-

cepted 1 voluntary surrender of medical license; placed 1 license on probation and restricted 3 medical licenses. The board denied reinstatement of 1 medical license and ordered 2 physicians not to practice until additional terms and conditions were met.

**Other Board Actions**

The Board adopted rules and regulations regarding the prevention of transimission of Hepatitis B Virus (HBV) and Human Innunodeficiency Virus (HIV) to patients.

In a joint effort, the Board of Medical Licensure and the Board of Nursing promulgated rules and regualtions governing Nurse Practitioners.

Further, amendments to the regulations were adopted which allows the issuance of a 90-day license for rotation for residents in approved post-graduate training programs out of state at a community hospital in Mississippi under certain conditions; and regualtions pertaining to the release of medical records. □

Members of the Board as of June 30, 1992 are:

**Mathew J. Page, MD,**  
Vice President  
1659 East Union Street  
Greenville, MS 38701  
Term: 7/1/86 - 6/30/92

**T. Steve Parvin, MD,**  
Secretary  
105 Doctors Park  
Starkville, MS 39759  
Term: 7/1/88-6/30/92

**Richard F. Riley, MD**  
1805 36th Street  
Meridian, MS 39305  
Term: 7/1/88 - 6/30/92

**John Purves McLaurin, Jr., MD**  
2200 S. Lamar Blvd, Ste C  
Oxford, MS 38655  
Term: 7/1/89 - 7/1/94

**W. W. Walley, MD**  
904 Mississippi Drive  
Waynesboro, MS 39367  
Term: 7/1/88 - 7/1/94

**Billy Wayne Long, MD**  
1421 North State Street  
Jackson, MS 39202  
Term 7/1/89 - 7/1/94  
Resigned : 4/10/92

**Joseph Rudolph Mitchell, MD**  
4333 15th Street, Suite A  
Gulfport, MS 39501  
Term 7/1/90 - 7/1/96

**John Langan Pendergrass, MD**  
PO Box 15729  
Hattiesburg, MS 39404  
Term: 7/1/90 - 7/1/96

**Walter H. Rose, MD,**  
President  
122 E. Baker Street  
Indianola, MS 38751  
Term: 7/1/90 - 3/30/96



# Today and Tomorrow The MSMA Belongs To You

If you are a physician practicing in Mississippi the Mississippi State Medical Association is your organization. It's the only organization which represents all Mississippi physicians....students, residents, women physicians, young physicians, established physicians, minority physicians and physicians in all specialties.

We can be proud that 83% of Mississippi physicians belong to the Mississippi State Medical Association...proud that so many Mississippi physicians feel a responsibility toward their colleagues and their profession. MSMA physicians support all three levels of organized medicine--their county medical society, the MSMA and the AMA.

Despite their diversity, Mississippi physicians have pretty much the same concerns. Providing the highest quality medical care possible. Ensuring access to care for all Mississippians. The freedom to practice without burdensome regulations. Fair health care legislation and equitable reimbursement. These issues are on the minds of Mississippi physicians and on the agenda of the Mississippi State Medical Association.

When you join MSMA or renew your existing membership, you are investing in your future. Read on. You might be surprised at the number of ways MSMA is working to improve the environment in

---

## MSMA is your voice in the Mississippi legislature and with governmental agencies

❖ When the Mississippi Legislature is in session, your MSMA staff is there, under the direction of the Council on Legislation and Board of Trustees elected by you, working for laws which benefit you and your patients.

❖ The MSMA maintains liaison with the Governor's office, the Mississippi State Department of Health, the Medicaid Division, the Insurance Department and other state agencies.

### MSMA quick fact # 1

Without MSMA efforts in the Mississippi Legislature, a tax on your license to practice would have been enacted to help balance the Medicaid budget.

### MSMA quick fact # 1

❖ The MSMA continues to advocate comprehensive public health legislation based on actions taken by the House of Delegates of the association elected by you.

❖ The Mississippi Medical Political Action Committee continues its crucial involvement in local, state and national elections. This committee scrutinizes the qualifications, voting records and platforms of all political candidates.

❖ MSMA member physicians represent the profession before health care committees and task forces appointed by the Governor and the Legislature. These committees formulate policy recommendations on Medicaid, cost control, medical licensure, rural health care and other issues.

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## MSMA is your voice with third party payors and allied health organizations

❖ MSMA staff assist physician members with problems relating to third party payors, Medicare and Medicaid.

❖ MSMA is active in representing physicians' concerns with other health provider groups such as the Mississippi Hospital Association, the Mississippi Nurses' Association, the Mississippi Pharmacists' Association, etc. MSMA physicians are involved in discussions with outside organizations regarding reform of our health care

### MSMA quick fact # 2

MSMA's leadership on public health issues such as school health education, AIDS and driver safety has increased the public's respect for all Mississippi physicians

### MSMA quick fact # 2

❖ MSMA has created a committee to help members deal with problems involving third party payors.

❖ MSMA maintains active relationships with the AMA and state specialty societies.

❖ MSMA seeks to address "hassles" you are having with third party payors.

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## MSMA is a source of information you need in today's complex environment

❖ MSMA members receive several newsletters which contain information on many subjects of interest to Mississippi physicians. The MSMA REPORT is sent monthly to members and discusses general topics including activities of MSMA officers and committees and timely developments in health care delivery.

❖ The MSMA Legislative Report is published



periodically during sessions of the Mississippi Legislature and keeps member physicians apprised of developments in the area of health care legislation.

- ❖ The *Journal of the Mississippi State Medical Association* is sent monthly to all MSMA members. The magazine contains articles exploring socioeconomic developments in medicine, scientific topics, physician editorials and practice management advice.

- ❖ The MSMA conducts an annual health forum and legislative reception in January for you to hear and discuss important legislative health issues with your senator and representative.

- ❖ MSMA Action Messages are sent to member physicians or legislative contact physicians when a major legislative or regulatory development occurs.

- ❖ An MSMA's Membership Directory containing the name, addresses and phone numbers of all MSMA members is provided annually to physicians and hospitals across Mississippi and others.

- ❖ MSMA has position papers on a number of key legislative health care issues which are available to any MSMA member.

- ❖ MSMA regularly provides informational brochures, flyers, etc. to its members. A recent example is a folder of information on the OSHA bloodborne pathogen standards mailed to concerned MSMA members. The folder included information physicians could use to respond to OSHA's requirements.

### **MSMA provides education opportunities in continuing Medical Education and medical socioeconomic issues.**

- ❖ The MSMA is involved in many continuing medical education activities. Scientific and medical socioeconomic sessions are held in conjunction with MSMA House of Delegates meetings. These sessions cover the latest medical techniques and socioeconomic and ethical issues important to Mississippi physicians.

- ❖ The MSMA is an accrediting agency for continuing medical education for institutions across Mississippi.

- ❖ *Journal MSMA* publishes scientific articles written by MSMA member physicians on a wide range of topics.

Every year the MSMA sponsors seminars and programs designed to help physicians improve management of their practices or learn about issues affecting health care delivery. A recent example is a series of workshops on Medicare, BRVS and CPT coding issues.

#### **MSMA quick fact # 3**

**MSMA has distributed informational materials about OSHA, CLIA and AR Keeping you informed about issues affecting you is one of our most important goals.**

#### **MSMA quick fact # 3**

### **MSMA is concerned about the public's opinion of physicians**

- ❖ MSMA seeks to encourage and publicize activities of its members dealing with community and civic improvements. MSMA annually presents a "Community Service Award" to a member which consists of a plaque and monetary award to a local civic organization chosen by the member.

- ❖ MSMA annually solicits and recognizes outstanding medical reporting by members of the communications media.

- ❖ MSMA conducts and publicizes a "Communi-Care Program" to encourage patients to address medical practice concerns with their personal physician or to call MSMA for assistance.

- ❖ MSMA produces patient education materials for members' offices on such health topics as AIDs, Smoking and Teenage Pregnancies.

#### **MSMA quick fact # 4**

**MSMA encourages effective reporting by the media on health issues and publicizes its members' activities to improve their communities**

#### **MSMA quick fact # 4**

### **MSMA is concerned about the health of all Mississippians**

- ❖ MSMA has studied health access issues in Mississippi: As a result "Health Access Mississippi" outlines a plan of action to address health access, quality and cost issues in Mississippi.

#### **MSMA quick fact # 5**

**MSMA has published Health Access Mississippi to address health access, quality and cost issues in Mississippi.**

#### **MSMA quick fact # 5**

### **MSMA is preparing to help you meet the challenges of the future**

- ❖ MSMA officers, physicians and staff are involved in strategic planning designed to assure that MSMA is prepared to meet the needs of its members in the future. Periodic membership surveys are conducted to determine your views on issues MSMA should be addressing.

# **MSMA Services**

## **Helping Mississippi Physicians Through People and Programs**

The right combination is needed if today's medical care challenges are to be unlocked and dealt with successfully. At **MSMA Services**, we think we have the right combination--informed people and sound programs.

As a subsidiary of the Mississippi State Medical Association, **MSMA Services** has combined people and programs to reflect its commitment to helping MSMA members and their staffs.

Proof that **MSMA Services** is succeeding is seen in the fact that 3 out of 4 Mississippi physicians - or their practices - participate either in one or several of our programs.

### **What areas of programming are offered by MSMA Services?**

#### **Practice management advice**

Whether it's individual practice consultation on "hassle factors" or an information/education program, **MSMA Services** is delivering help to Mississippi physicians and is getting good feedback on its expanding activity in the areas of reimbursement, coding, billing and patient relations.

Staff expertise is built by contact with various resources. Answers and solutions are furnished to practice-specific inquiries and in special workshops and conferences held throughout the state.

#### **Assistance with health and other insurance needs**

Since MSMA Benefit Plan and Trust was founded in 1983, **MSMA Services** has served as its administrator. **MSMA Services'** staff counsel association members on their health insurance needs and questions.

Other low cost MSMA member insurance programs are furnished in various areas such as health, life, disability, workers' compensation, annuities. Sponsored coverages are selected for their stability, benefit features designed specifically for physicians and cost-effectiveness.

#### **Help for specialty groups**

A rapidly growing **MSMA Services** support activity is helping Mississippi medical specialty groups carry out their organizational programs.

Administrative/executive assistance is provided to the state societies of psychiatrists, surgeons, internists, radiologists and anesthesiologists.

#### **And that's not all**

Each year, additional programs are initiated to serve physicians and their practices. There's a billing and collection service and claim form 1500 supply service.

#### **Who do you call?**

Direct your inquiries to **MSMA Services**, PO Box 5229, Jackson, MS 39292-5229 or telephone 354-5433 or 1-800-898-0251.





*Photo courtesy of the Mississippi Department of Economic and Community Development.*

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## The President's Page

WILLIAM C. GATES, MD

### REFORM, RESOLVE AND REAFFIRMATION

"I believe that man will not merely endure. He will prevail. He is immortal, not because he alone among creatures has an inexhaustible voice, but because he has a soul, a spirit capable of compassion and sacrifice and endurance."

William Faulkner

On the occasion of his acceptance  
of the 1949 Nobel Prize

**T**he campaign, characterized in a New York tabloid as involving "a wimp, a wonk, and a wacko," is over and the wonk won. President Clinton, more than once, has been described as a "policy wonk" whose initial, immediate agenda includes, as the top three items, stimulating economic growth, reducing the deficit and health system *reform*.

The same three issues will be top priorities for the 103rd Congress (which will be known as the "half and half" congress—half newly-elected and half nearly-dead). These three problems will be particularly vexing for the Clinton transition team and ultimately, the Clinton Administration because the issues are interwoven and *will* generate policy conflicts. Think about it— a major expansion of access to health care coverage may be difficult to sell until the economy improves. The rising health care costs are already tagged as a drag on American competitiveness in international markets, as well as a big component of the progressively rising federal deficit which, because of its hugeness, casts a shadow over options for economic stimulus programs as well as the notion of extending health insurance coverage to the uninsured.

There are a number of players in Congress and in the private sector that will

*(Continued on page 56)*

## LETTER TO GOD

Dear God:

I really hate to bother you with such trivial things, but I don't know any responsible person here on earth that might be able to help me so I thought I would turn to you for help. You see medical care and medical practice in our country is just getting to be a real mess and no one person is in charge. I'd like to do something about it but I am so small and the problems are so large that I don't know with whom, or how, to even begin.

I know that most of our problems are centered around the federal government, but there is no one person or one group in charge there that will or can help us. God, I always thought that you were the omniscient, omnipotent one but so help me it looks like our federal government thinks it is now. It appears that things are just before getting worse with the new party in power that is made up of more special interest groups than ever and all of whom are waiting to pressure the powers that be for what they feel is their deserved plum. Yes, I hear and read that medical reform is one of their hot topics, and that's one of the things I wanted to talk to you about. You see medical reform done in Washington is only compounding the problems that are already worrying me. It is said that for each treatment or what they call patient encounter there is an average of ten (10) pieces of paper generated. You can get some idea about how much worse it can get from this. Only in a bureaucracy such as ours does it take more time with paperwork than it does seeing and treat-

ing our patients.

God, I know that as dedicated doctors we are supposed to do our share of charity work and I do my best, but I've got real problems with this. You see a third of my patients are on welfare and another third are on welfare and Medicare together. Welfare only pays 40% of my bill and it's really hard to make that other third (less the non-paying) take up the slack. As you know 40% payments won't even pay my help and overhead. So Lord, would you try to help me someway along these lines for I do want to do my part for the sick and unfortunates and yet I don't want to quit like a growing number of physicians in my state have done because of the low pay and the government's seeming uncaring attitude.

I don't want to worry you, God, but what on earth am I to do about the new clinical laboratory rules and the new OSHA regulations. Our all-knowing and all-seeing government in its infinite wisdom has really made a mess of our offices. In these almost forty years of practice, I have had over one-half million patient visits and have yet to get blood, urine, or pus in either my eyes or the eyes of my assistants. Yet the federal government mandates (under heavy fine for disobedience) that I have to have an eyewash center in my office. Now, Lord, does this sound like progress to you? Another example of all this foolishness is that I have to gown-up, mask-up, glove-up, and put on goggles to draw blood from a screaming child who is scared to death by all this

*(Continued on page 57)*

The editorial opinions expressed in this Journal are those of the indicated author. Editorial opinions are not expressions of the views, or official policies of The Mississippi State Medical Association. We encourage the membership to submit letters for publication regarding any opinion expressed or information contained in the Journal.



## President's Page

(Continued from page 54)

attempt to influence the health system reform debate and to modify the rate and nature of change as the final product is created. Organized medicine seems well-positioned to be given a place at the table and Clinton's health advisors have repeatedly expressed interest in consulting with key stakeholders, not only during the campaign but currently, also. The AMA will have to remember, however, the ancient oriental proverb that states, "Once your place at the table is assured, you must then be sure that *you* are *not* the *main course*!"

The *resolve* that we must have as physicians will necessarily embrace the concept that the status quo is no longer acceptable—to paraphrase George Lundberg, *JAMA* editor, the aura of inevitability is upon us and it is morally, ethically and economically impossible to accept the fact that so many Americans are uninsured or gravely underinsured. "A long-term crying need has developed into a national moral imperative and now into a pragmatic necessity as well."

The AMA supports reform concepts that would expand access while maintaining the patient's freedom of choice and physician autonomy that avoids interference with clinical judgment. The AMA is opposed to reform plans that would impose federal price controls on physicians and hospitals, as well as establish arbitrary budget caps on health spending (global budgets). We will have to be innovative and all players may have to compromise and, to quote

Lundberg again. "the United States will have to change its health care thinking from chaotic, proprietary, fragmented, self-serving and short-sighted to systematic, strategic and long-term."

While this debate goes on, probably into the '94 elections and beyond, we physicians will find some relief and respite in *reaffirmation* of our professionalism and continued concern, compassion and commitment to provide medical care with respect for human dignity, both our patient's and our own. In the current environment, it is imperative that the government recognize medical professionalism and resolve anti-trust issues that obviate self-regulation and negate the ability to negotiate. In the absence of those prerogatives, physicians will be as little Davids with an empty sling shot going up against the Goliaths of hospital networks, the insurance industry and other corporate entities. We need to remind the public and the politicians that in the "good old days" of professional sovereignty many "individual, autonomous physicians carried the practice of medicine to a peak of quality, cost-effectiveness and compassion which is unlikely to be found again when this revolution has run its course and the health care industry is ruled by corporate or governmental authority." (The quote is from Dr. Lamar Weems in "Professionalism Under Siege" at a seminar at Millsaps College, 1988.)

The AMA will aggressively lobby for physician self-regulation provisions and relief from some of the anti-trust laws as well as seeking the Federal Trade Commission's acceptance

of a variety of self-regulatory initiatives. The AMA is also seeking a new partnership with the executive branch which involves greater reliance on and input from the medical profession for the development of medical decision-making criteria and a more formal negotiations role on Medicare policies. On a state level, the physicians of Mississippi perhaps should consider reactivating our previously ill-fated IPA to have available for negotiating purposes.

I will close with a quote from Dr. Weems' essay mentioned already - *vide supra*.

"In a hostile and cynical world, treasures must be protected. Professionalism is a treasure which has great value to the various professions and to the public. Professionals of all disciplines should be jealous of their prerogatives, attentive to their obligations and vigilant in maintaining the power required to protect their inheritance. Attention to business is usually required."

Even though we must and should pay attention to business, let us resolve and reaffirm that reform will be created in a crucible of caring.

I hope my note finds you and yours doing well ....

Best regards,  
Bill

**Editorial**  
(Continued from page 55)

Martian outfit mandated by the federal government.

But Lord, I'd really like you to help me on this one because it just isn't fair to me or to my patients. You know I don't do much laboratory work in my office—less than 2000 procedures a year and with the new government regulations it will cost me more than I make from them to do them. I am selling my

laboratory equipment. This translates into a great inconvenience to my patients and for me. This means, Lord, that if you come in my office with the bellyache and I need a blood count to determine whether this is appendicitis or just a bad case of stomach virus you're going to have to find a ride and go 10 miles to the hospital laboratory; get the test; and then come back the 10 miles for me to treat you. Lord, you probably never had a bad stomachache, but I can

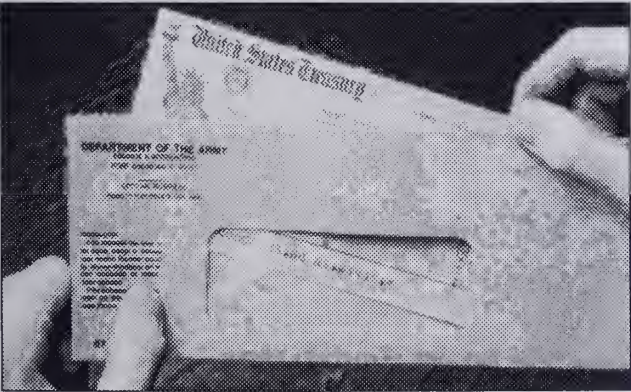
guarantee your stomach won't feel any better after all that running around. Would you please speak to someone somewhere and see if you can get some of these regulations changed?

Thanks, God, for listening to me and I surely would appreciate any help you can give me. One last thing, thanks for letting me be a physician.

**Joseph E. Johnston, MD**  
Associate Editor

# ANESTHESIOLOGISTS AND SURGEONS: COULD YOU USE AN EXTRA \$9,000?

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# Medical Organization

## Dr. Ed Thompson Appointed Interim State Health Officer

The Board of Health voted unanimously to appoint Dr. Ed Thompson as Interim State Health Officer effective January 1, 1993, at a special meeting December 2, 1992. Dr. Thompson said that the unanimous vote showed the Board's strong support not just to him, but for the agency as a whole.

"It is important to note that the Board looked inside the agency for an interim state health officer," he said. "That shows their confidence in the agency and the people who work here."

Dr. Thompson said he agreed to accept that position on the condition that the Board of Health wanted someone not just to mark time but to move the agency forward. "When I was talking with the Board members about this appointment, I made sure they knew this was one of the best state health departments in the country," he said. "I don't want to change that, except to make it better."

Dr. Thompson, who already serves as chief of the Bureau of Preventive Health and State Epidemiologist, said he plans "no basic changes in the agency's direction. Any changes will be adjustment-type fine-tuning, things that probably would have been

done anyway."

One of his first priorities is to work with the Legislature to get the budget request fully funded. Given that Legislative priority, and he also plans to visit as many of the district and county offices as possible.

"One real strong belief of mine is the District system," he said. "I would like to improve the way we use it and increase local involvement in areas outside personal health. Also the District system has the ability to provide more accountability to the Central Office without any changes in the structure. We just need to use what's there."

Plans also call for increasing the role of District Staff in the development of agency policy. "I'd like to involve them in discussions in the beginning," he said. "We also need more help from them in carrying out the policies." He hopes bringing the District Staff in will "help them feel more like a part of the team. It will also make our policies more practical, which helps make better policy."

Dr. Thompson said he also appreciates that the Board gave him authority to appoint a deputy state health officer. Dr. B.J.

Phillips, chief, Bureau of Health Resources and Laboratory, will fill that role.

"Dr. Phillips and I have worked closely together on many projects," Dr. Thompson said. "She'll fill in during my absences and lend her expertise in many areas, particularly those in her Bureau."

At the November meeting, the Board of Health also appointed three members to conduct a nationwide search for a permanent state health officer. Dr. Maurice James, Linda Gholston, and Frank Genzer. Board Chairman Don Felts, who will assist with the search, said he expects the process to take several months, with June 1993 as the target date for appointing a new state health officer.

Dr. Thompson received his MD degree from the University of Mississippi School of Medicine, and his MPH from Johns Hopkins University School of Hygiene and Public Health. He is board certified in Public Health and General Preventive Medicine. He is President, Council of State and Territorial Epidemiologists, President-elect, Mississippi Public Health Association, and a member of the Advisory Committee on Immunization Practice, U.S. Public Health Service. Dr. Thompson is a member of Central Medical Society, the MSMA, and the AMA. □

## MSMA 1993 SOCIO-ECONOMIC AND LEGISLATIVE FORUM HELD JANUARY 19th IN JACKSON



*John P. Seward, MD, Member, AMA Board of Trustees and Chair, AMA Technical Advisory Committee on Health System Reform*



*Above, John J. McGrath, MD, Washington, DC. Below, Brian Martin, Office of Congressman Gene Taylor*



The 1993 Medical Socioeconomic Forum and Legislative reception was held at the Jackson Ramada Coliseum Hotel on January 19, 1993. Forum participants represented the Mississippi State Medical Association, the Mississippi Hospital Association, the Mississippi Association of Hospital Governing Boards and the Mississippi State Medical Association Auxiliary.

The program began at a noon luncheon with over 300 present. Mississippi State Medical Association President, William C. Gates, Jr., MD, presided over the opening session introducing Dr. Carl Hammerschlag from Phoenix, Arizona, guest speaker. Dr. Hammerschlag, a psychiatrist in private practice spoke on the topic, "Success is a Leap of Faith."

A Yale-trained psychiatrist, Dr. Hammerschlag spent almost twenty years as a physician with Native Americans in the Southwest. There, many of his medical school assumptions were challenged, and he learned that healing has a much to do with one's active participation in the process as with the creation of technology.

A master storyteller, Dr. Hammerschlag, led his audience on a journey of self-discovery that allowed each to see familiar things in new ways. He related many stories about how the practice of medicine has changed over the years because some chose to look at things in a different way. Dr. Hammerschlag further commented that each person now has a choice about how they allow all the changes in America's healthcare system to affect them.

The afternoon session speakers discussed many of the proposed changes in the current healthcare system. Dr. J. Edward Hill of Hollandale, presided over the first portion of the afternoon session.

The program began with Brian Martin, Legislative Assistant from the office of Congressman Gene Taylor. Mr. Martin discussed the health reform policy and goals of the House Conservative Democratic Forum. He particularly addressed the issue of managed competition.

Dr. John J. McGrath of Washington, contin-



ued the discussion by addressing the health reform policy and goals of President Bill Clinton. Dr. McGrath, served as a member President Clinton's transition team on the health care advisory of committee. Dr. McGrath stated that we would definitely see a health reform plan presented to the Congress by President Clinton in the first 100 days. This plan, however, stated Dr. McGrath though not complete would include the major goals in each area of reform.

Dr. John P. Seward, Member, AMA Board of Trustees and Chair, AMA Technical Advisory Committee of Health System Reform spoke during the second portion of the afternoon session. Dr. Seward stated that the AMA has been actively involved with the Clinton administration in the development of health system reform. He further stated that AMA's Health Assess America program is continually being refined to address all issues in health system reform.

All Forum speakers expressed concerns over the proposal of "global budgeting" and what this would mean and how it would be used in health system reform.

The afternoon meeting concluded with an overview of the 1993 Mississippi Legislative Session by MSMA Director of Legislative Affairs Clare Hester.

More than 125 Senators and Representatives and approximately 150 physicians, spouses and MSMA staff members attended the Legislative Forum and evening reception. □



*William C. Gates, Jr., MD, MSMA President*

*Patricia Ainsworth, MD, left, president-elect of the Mississippi Psychiatric Association and Robert C. Clingan, MD, of Vicksburg greet luncheon speaker, Carl Hammerschlag, MD, right, after his presentation. Dr. Hammerschlag is a psychiatrist in private practice from Phoenix, Arizona.*





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# From the University of Mississippi Medical Center

## Dr. Halaris Appointed Psychiatry Department Chairman

Dr. Angelos E. Halaris has been appointed chairman of the Department of Psychiatry and Human Behavior at the University of Mississippi Medical Center. He assumes the post March 1.

Dr. Halaris succeeds Dr. Edgar Draper, chairman since 1975. Dr. Draper will remain on the faculty.

UMC Vice Chancellor Dr. Norman C. Nelson announced the appointment following approval of the Board of Trustees, Institutions of Higher Learning.

"We are very pleased to have attracted a medical educator of Dr. Halaris' caliber to head this important department," said Dr. Nelson. "He has exceptional credentials in academic medicine and a highly productive research record."

Dr. Halaris is a professor of psychiatry and pharmacology and vice chairman of the Department of Psychiatry at Case Western Reserve University School of Medicine in Cleveland, Ohio. He also is the director of the Department of psychiatry at MetroHealth Medical Center in Cleveland.

Prior to joining the Case Western Reserve faculty, Dr. Halaris held teaching positions at the University of Chicago School of Medicine and UCLA School of Medicine. He also has served as the director of the psychiatry residency training program at the MetroHealth Medical Center.

A Fulbright Scholar, Dr. Halaris earned a MD/PhD at the University of Munich Medical School in Munich, West Ger-

many. He completed his residency in psychiatry and a fellowship in psychopharmacology at the University of Chicago.

A native of Athens, Greece, Dr. Halaris served in the Greek Army in 1971. He is the author of a book on *Chronobiology and Psychiatric Disorders* and more than 100 published papers, many of which deal with his principal research interests in depression, schizophrenia, anxiety disorder and drugs used to treat these psychiatric illnesses. He has made numerous presentations at national and international conferences as well as radio and TV shows. □

**The Delta Region AIDS Education and Training Center** grant is one of 17 federally funded for specialized comprehensive HIV/AIDS Education and Training in Arkansas, Louisiana, and Mississippi. Educational offerings are available in six disciplines - medicine, nursing, dentistry, infection control, mental health, and social work. Physicians, nurses, and health-related professionals are available to visit your area and provide educational services. Please include us in your next meeting. Additional information may be obtained by calling the Division of Infectious Diseases, University of Mississippi Medical Center.

**Jan M. Evers, RN, MN, Resource Center Director**

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2500 North State Street, Jackson, MS 39216-4505

## Dr. Ho Invited To Serve On Board Of Scientific Counselors

Dr. Ing K. Ho, professor and chairman of the Department of Pharmacology and Toxicology at the University of Mississippi Medical Center, has been invited to serve on the Board of Scientific Counselors of the Agency for Toxic Substances and Disease Registry (ATSDR).

The invitation was issued by Dr. Louis Sullivan, U.S. Secretary of Health and Human Services.

The board advises the ATSDR on the adequacy of science in

agency-supported research and recommends research programs and conference support for grants to institutions.

The 11-member board consists of authorities in medicine, toxicology, pharmacology, engineering, industrial hygiene, environmental chemistry, epidemiology, hydrology and environmental health. Dr. Ho has been invited to serve a four-year term.

A member of the UMC faculty since 1975, Dr. Ho was ap-

pointed chairman of UMC's Department of Pharmacology and Toxicology in 1982. He is a graduate of the University of California in San Francisco where he earned a PhD in biochemistry. Dr. Ho also holds a BS in chemistry from the National Taiwan University in Taipei, Taiwan.

His postgraduate training includes study as a research pharmacologist in the Department of Pharmacology at the University of California and an associate research position in the Department of Anesthesiology at the Baylor College of Medicine in Houston. □



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# New Members

**Bianco Anthony C.**, Hattiesburg. Born Brooklyn, New York, July 15, 1948; MD, Louisiana State University School of Medicine, New Orleans, LA, 1986; psychiatry residency, Institute of Living, Hartford, CT, 1986-89 and child & adolescent psychiatry, same, 1989-91; elected to membership by South Mississippi Medical Society.

**Ccmelicek, John T.**, Purvis. Born Brno, Czechoslovakia, September 16, 1960; MD, University of Alberta Faculty of Medicine, Edmonton, Canada, 1985; family medicine residency, McGill University, Montreal, Quebec, Canada, 1985-87; elected by South Mississippi Medical Society.

**Jenkins Ronald A.**, Gulfport. Born Lafayette, LA, August 3, 1949; MD, University of Mississippi School of Medicine, Jackson, MS, 1981; interned one year, University Medical Center, Lafayette, LA; anesthesiology residency, UMC, Jackson, MS, 1992-84; anesthesiology fellowship, LSU School of Medicine, Shreveport, LA, 1985; elected by Coast Counties Medical Society.

**Jimenez-Agosto Jaime**, Hattiesburg. Born San Juan, Puerto Rico, March 7, 1960; MD, University of Puerto Rico, Medical Sciences Campus, San Juan, Puerto Rico, 1983; pediatric internship, same, 1983-84

and rotating internship, same 84-85; ophthalmology residency, same, 1987-88; fellowship in vitreoretinal diseases and surgery, Hermann Eye Center, Houston, TX, 1990-92; elected by South Mississippi Medical Society.

**Johnson, Jeffrey A.**, Hattiesburg. Born New Orleans, LA,

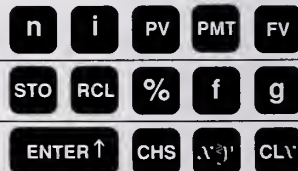
October 16, 1958; MD, Louisiana State University School of Medicine, Shreveport, LA, 1984; internal medicine residency, Ochsner Foundation Hospital, New Orleans, LA 1984-87; elected by South Mississippi Medical Society.

**Kumar, Vinay**, Hattiesburg. Born Chhindwara, India, De-

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ember 19, 1952; MD, Government College, Nagpur, India 1974; interned one year, same; general surgery residency, same, 1976-85; elected by South Mississippi Medical Society.

**Nelson, Scott E.**, Cleveland. Born Greenville, MS, November 30, 1963; MD, University of Mississippi School of Medicine, Jackson, MS, 1989; interned and family practice residency, University Medical Center, Jackson, MS, 1989-92; elected by Delta Medical Society.

**McKenzie Antronette L.**, McComb. Born Cincinnati, Ohio, October 17, 1951; MD, Wright

State University School of Medicine, Dayton, Ohio, 1985; interned and medicine residency, same, 1985-91; elected by South Central Medical Society.

**Rigsby Reginald D.**, Jackson. Born Jackson, MS, August 2, 1958; MD, Meharry Medical College School of Medicine, Nashville, TN, 1982; interned one year, Wayne State University, Detroit, Michigan; surgery internship, one year, South Baltimore Hospital, Baltimore, MD; family medicine residency, University of Maryland, Baltimore, MD, 1984-86; elected by Central Medical Society.

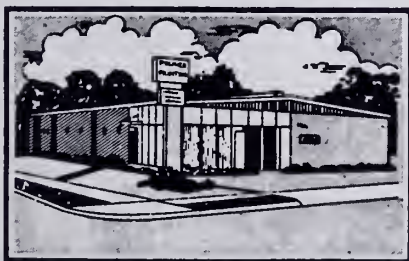
**White, Clinton B.**, Hattiesburg.

Born Jackson, MS, June 4, 1958; MD, University of Mississippi School of Medicine, Jackson, MS, 1986; pediatric residency, UMC, Jackson, MS 1986-89; neonatology fellowship, University of Louisville, Louisville, KY, 1992; elected by South Mississippi Medical Society.

**Willis, Walter L.**, Philadelphia. Born Indianola, MS, August 27, 1959; MD, University of Mississippi School of Medicine, Jackson, MS, 1986; family medicine residency, University of Alabama Medical Center, Tuscaloosa, AL, 1986-89; elected by East Mississippi Medical Society. □

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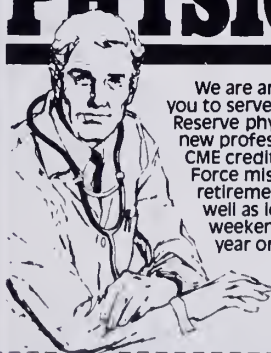
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# Deaths

- |                              |  |
|------------------------------|--|
| <u>Guy D. Campbell, MD</u>   | Jackson. Born Lauderdale, MS, October 15, 1915; MD, University of Mississippi School of Medicine, Jackson, MS and Harvard Medical School, Boston, MA 1949; interned one year Charity Hospital, New Orleans, LA; residency in Chest Disease one year, Mississippi State Sanatorium and two years, Internal Medicine, V. A. Hospital, New Orleans, LA; member of Central Medical Society; died January 26, 1993, age 77. |
| <u>Louis A. Farber, MD</u>   | Jackson. Born in Cordell, OK, January 4, 1921; MD, University of Mississippi School of Medicine, Jackson, MS 1959; interned and orthopedic residency, same, 1959-64; member of Central Medical Society; died January 11, 1993, age 72.   |
| <u>J. Dan Mitchell, MD</u>   | Jackson. Born Union City, TN, July 6, 1925; MD, University of Mississippi School of Medicine and University of Tennessee School of Medicine, Memphis, TN, 1956; interned one year Saint Joseph Hospital, Memphis, TN; member of Central Medical Society; died December 2, 1992, age 67.  |
| <u>W. H. Parker, MD</u>      | Heidelberg. Born Philadelphia, MS, October 18, 1916; MD, University of Tennessee College of Medicine, Memphis, TN, 1941; interned one year, Baptist Memorial Hospital, Memphis, TN; member of South Mississippi Medical Society; died October 30, 1992, age 76.  |
| <u>John Neil Turnage, MD</u> | Aberdeen. Born New Hebron, MS, May 16, 1926; MD, University of Mississippi School of Medicine & University of Tennessee College of Medicine, Memphis, TN, 1956; interned one year, Methodist Hospital, Memphis, TN; member of Northeast Mississippi Medical Society; died December 10, 1992, age 66. □   |

## FOR COMMENTS OR QUERIES

The Editors of *Journal MSMA* invite you to comment on any material that appears in or is absent from the publication. If you have a query or comment, please send it to: The Editor, *Journal MSMA*, PO Box 5229, Jackson, MS 39296-5229.



# Personals

**William T. Avara, III**, announces the relocation of his office for the practice of General, Thoracic and Vascular Surgery to: Doctors Plaza, 4211 Hospital Road, Suite 101, Pascagoula.

**Donald W. Benefield** of Gulfport has been certified by the American Board of Ophthalmology.

**P. Temple Carney** has associated with Central Psychiatry & Psychology Clinic, 4 River Bend Place, Jackson for the

practice of child, adolescent, and adult psychiatry.

**Maxwell C. Cooke**, has associated with **Jimmy R. Chism** and **David J. Williams**, The Women's Clinic of New Albany, in the practice of Obstetrics and Gynecology.

**Samuel Crosby**, **Wayne Hughes**, and **Michael May** announce the opening of: The Family Practice Clinic, 110 Millsaps Drive, Methodist Medical Park, Hattiesburg.

**Richard J. Cunningham**, has associated with Community Medical Center of Lucedale in the practice of family medicine.

**Deborah J. Downing** of Meridian has been certified by the American Board of Internal Medicine.

**Randy Easterling** a family physician in Vicksburg has earned a certificate as a medical review officer from the American Association of Medical Review Officers.

## Physicians' Recognition Award



Six MSMA members were named recipients of the AMA Physicians' Recognition Award in December 1992. This award is presented by the American Medical Association to Physicians who have voluntarily completed a specified number of continuing medical education hours. These individuals are presented below by medical society.

Central Medical Society  
**Joseph H. Robinson, MD**

North Mississippi Medical Society  
**Pravinchandra P Patel, MD**

South Central Mississippi Medical Society  
**Elmo P. Gabbert, MD**  
**Daniel T. Keel, Jr., MD**

South Mississippi Medical Society  
**James W. Holmes, MD**  
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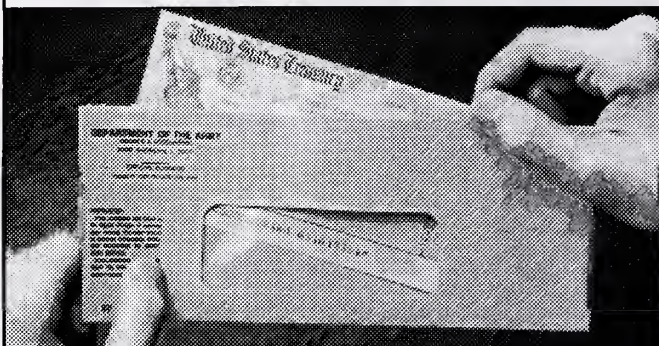
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### Personals/continued

**William R. Fellows** of Biloxi has been appointed Medical Director of the Addictive Disease Unit and Recovery Resources at Gulf Oaks Hospital.

**Todd L. Fulcher** has associated with **Glenn F. Morris** and **Cynthia E. Allen** for the practice of family medicine, at 1029 River Oaks Drive, Jackson.

**Gerry Ann Houston** a medical oncologist and hematologist of Jackson, has been elected to Fellowship in the American College of Physicians. She was guest speaker at a Breast Cancer Awareness Seminar held recently in Crystal Springs.

**Stephen C. Lambert**, medical director of the Southeast Mississippi Rural Health Initiative in Seminary, was named the "Outstanding Clinician of the Year" by the Mississippi Primary Health Care Association.

**Ronald R. Lubritz** of Hattiesburg was recently appointed clinical professor of medicine/dermatology at Tulane University School of Medicine, New Orleans.

**James N. McQueen** announces the opening of his office for the practice of dermatology, 348 Crossgates Boulevard, Brandon.

**R. Bruce Newell** has associated with **Fred M. Sandifer** and **William E. Anderson**, Greenwood Orthopedic Clinic, in the practice of orthopedic surgery.

**Buddy Savoie** of Jackson was the featured lecturer on suture reconstruction of the shoulder at the AANA Fall Course during November, in Monterey, California.

**Carol Scott-Conner**, UMC professor of surgery, and **Terrance Hall**, UMC assistant professor of surgery recently spent two weeks in China as part of a team of five surgeons from across the U.S. teaching

Personals/continued

operative laparoscopy. The team spent three days in both Shanghai and Beijing operating and teaching. In the two cities the team performed 11 operations, all successfully. The trip was organized by Dr. Berci of Cedars-Sinai Medical Center in Los Angeles under the aegis of SAGES, the national surgical endoscopy society.

**Billy Walker**, dermatopathologist of Jackson, was a panelist for the program "Self Assessment in Dermatopathology" given by the American Academy of Dermatology at their annual national meeting in San Francisco in December, 1992.

**Steven C. Williams and Martin L. Howard, Jr**, General & Vascular Surgery Specialists, PA, announce the relocation of their offices to 1311 Aston Avenue, McComb. □

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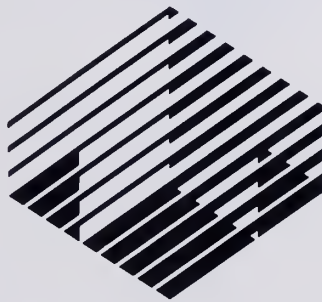
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The Mississippi DDS is recruiting physicians for part-time employment in the Jackson Office. Job requires review of medical reports for determination of benefit eligibility under Social Security criteria. Board certified/eligible psychiatrists, pediatricians, pulmonologists, cardiologist and neurologists are needed. Flexible work schedules. For information contact Deborah Warriner at 601-923-2153.



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Bristol-Myers Squibb Company - Pravachol .....	covers III and IV
CancerPay Plus .....	4
CompHealth .....	69
CompuMed .....	58
Deposit Guaranty Investments .....	41
Disability Determination .....	70
Doctors Insurance Reciprocal .....	44
Eli Lilly & Co. - Humulin .....	cover II
Medical Assurance Co. of MS .....	5
Medley & Company .....	64
MS Emergency Association .....	71
MS Physicians Insurance Company .....	40
MSMA Benefit Plan & Trust.....	8
Premier Printing .....	63
PRI-MED, Inc. ....	71
The Doctors' Company .....	53
Trustmark .....	69
US Air Force .....	63
US Air Force Reserve .....	65
US Army Active .....	68
US Army Reserve .....	57



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**WARNINGS**

**Enzymes:** HMG-CoA reductase inhibitors, like some other lipid-lowering therapies, have been associated with biochemical abnormalities of liver function. Increases of serum transaminase (ALT, AST) values to more than three times the upper limit of normal occurring on 2 or more (not necessarily sequential) occasions have been reported in 1.3% of patients treated with pravastatin in the U.S. over an average period of 18 months. These abnormalities were not associated with cholestasis and did not appear to be related to treatment duration. In some patients in whom these abnormalities were believed to be related to pravastatin and who were discontinued from therapy, the transaminase levels usually fell slowly to pretreatment levels. These biochemical findings are usually asymptomatic although worldwide experience indicates that anorexia, weakness, and/or abdominal pain may also be present in rare patients.

As with other lipid-lowering agents, liver function tests should be performed during therapy with pravastatin. Serum aminotransferases, including ALT (SGPT), should be monitored before treatment begins, every six weeks for the first three months, every eight weeks during the remainder of the first year, and periodically thereafter (e.g., about six-month intervals). Special attention should be given to patients who develop increased transaminase levels. Liver function tests should be repeated to confirm an elevation and subsequently monitored at more frequent intervals. If increases in AST and ALT equal or exceed three times the upper limit of normal and persist, on therapy should be discontinued. Persistence of significant aminotransferase elevations following discontinuation of therapy may warrant consideration of liver biopsy.

Active liver disease or unexplained transaminase elevations are contraindications to the use of pravastatin (see CONTRAINDICATIONS). Caution should be exercised when pravastatin is administered to patients with a history of liver disease or heavy alcohol ingestion (see CLINICAL PHARMACOLOGY: Pharmacokinetics/Metabolism). Such patients should be closely monitored, started at the lower end of the recommended dosing range, and treated to the desired therapeutic effect.

**Skeletal Muscle:** Rhabdomyolysis with renal dysfunction secondary to myoglobinuria has been reported with pravastatin and other drugs in this class. Uncomplicated myalgia has also been reported in pravastatin-treated patients (see ADVERSE REACTIONS). Myopathy, defined as muscle aching or muscle weakness in conjunction with increases in creatine phosphokinase (CPK) values to greater than 10 times the upper limit of normal was reported to be possibly due to pravastatin in only one patient in clinical trials (<0.1%). Myopathy should be considered in any patient with diffuse myalgias, muscle tenderness or weakness, and/or marked elevation of CPK. Patients should be advised to report promptly unexplained muscle pain, tenderness or weakness, particularly if accompanied by malaise or fever. **Pravastatin therapy should be discontinued if markedly elevated CPK levels occur or myopathy is diagnosed or suspected. Pravastatin therapy should also be temporarily withheld in any patient experiencing an acute or serious condition predisposing to the development of renal failure secondary to rhabdomyolysis, e.g., sepsis; hypotension; major surgery; trauma; severe metabolic, endocrine, or electrolyte disorders; or uncontrolled epilepsy.**

The risk of myopathy during treatment with lovastatin is increased if therapy with either cyclosporine, gemfibrozil, erythromycin, or niacin is administered concurrently. There is no experience with the use of pravastatin together with cyclosporine. Myopathy has not been observed in clinical trials involving small numbers of patients who were treated with pravastatin together with niacin. One trial of limited size involving combined therapy with pravastatin and gemfibrozil showed a trend toward more frequent CPK elevations and patient withdrawals due to musculoskeletal symptoms in the group receiving combined treatment as compared with the groups receiving placebo, gemfibrozil, or pravastatin monotherapy. Myopathy was not reported in this trial (see PRECAUTIONS: Drug Interactions). One patient developed myopathy when clofibrate was added to a previously well tolerated regimen of pravastatin; the myopathy resolved when clofibrate therapy was stopped and pravastatin treatment continued. **The use of fibrates alone may occasionally be associated with myopathy. The combined use of pravastatin and fibrates should generally be avoided.**

**PRECAUTIONS**

**General:** Pravastatin may elevate creatine phosphokinase and transaminase levels (see ADVERSE REACTIONS). This should be considered in the differential diagnosis of chest pain in a patient on therapy with pravastatin.

**Homozygous Familial Hypercholesterolemia.** Pravastatin has not been evaluated in patients with rare homozygous familial hypercholesterolemia. In this group of patients, it has been reported that HMG-CoA reductase inhibitors are less effective because the patients lack functional LDL receptors.

**Renal Insufficiency:** A single 20 mg oral dose of pravastatin was administered to 24 patients with varying degrees of renal impairment (as determined by creatinine clearance). No effect was observed on the pharmacokinetics of pravastatin or its 3 $\alpha$ -hydroxy isomeric metabolite (SQ 31,906). A small increase was seen in mean AUC values and half-life (t<sub>1/2</sub>) for the inactive enzymatic ring hydroxylation metabolite (SQ 31,945). Given this small sample size, the dosage administered, and the degree of individual variability, patients with renal impairment who are receiving pravastatin should be closely monitored.

**Information for Patients:** Patients should be advised to report promptly unexplained muscle pain, tenderness or weakness, particularly if accompanied by malaise or fever.

**Drug Interactions:** Immunosuppressive Drugs, Gemfibrozil, Niacin (Nicotinic Acid), Erythromycin: See WARNINGS: Skeletal Muscle.

**Antipyrine:** Clearance by the cytochrome P450 system was unaltered by concomitant administration of pravastatin. Since pravastatin does not appear to induce hepatic drug-metabolizing enzymes, it is not expected that any significant interaction of pravastatin with other drugs (e.g., phenytoin, quinidine) metabolized by the cytochrome P450 system will occur.

**Cholestyramine/Colestipol:** Concomitant administration resulted in an approximately 40 to 50% decrease in the mean AUC of pravastatin. However, when pravastatin was administered 1 hour before or 4 hours after cholestyramine or 1 hour before colestipol and a standard meal, there was no clinically significant decrease in bioavailability or therapeutic effect. (See DOSAGE AND ADMINISTRATION: Concomitant Therapy.)

**Warfarin:** In a study involving 10 healthy male subjects given pravastatin and warfarin concomitantly for 6 days, bioavailability parameters at steady state for pravastatin (parent compound) were not altered. Pravastatin did not alter the plasma protein-binding of warfarin. Concomitant dosing did increase the AUC and C<sub>max</sub> of warfarin but did not produce any changes in its anticoagulant action (i.e., no increase was seen in mean prothrombin time after 6 days of concomitant therapy). However, bleeding and extreme prolongation of prothrombin time has been reported with another drug in this class. Patients receiving warfarin-type anticoagulants should have their prothrombin times closely monitored when pravastatin is initiated or the dosage of pravastatin is changed.

**Cimetidine:** The AUC<sub>0-12h</sub> for pravastatin when given with cimetidine was not significantly different from the AUC for pravastatin when given alone. A significant difference was observed between the AUC's for pravastatin when given with cimetidine compared to when administered with antacid.

**Digoxin:** In a crossover trial involving 18 healthy male subjects given pravastatin and digoxin concurrently for 9 days, the bioavailability parameters of digoxin were not affected. The AUC of pravastatin tended to increase, but the overall bioavailability of pravastatin plus its metabolites SQ 31,906 and SQ 31,945 was not altered.

**Gemfibrozil:** In a crossover study in 20 healthy male subjects given concomitant single doses of pravastatin and gemfibrozil, there was a significant decrease in urinary excretion and protein binding of pravastatin. In addition, there was a significant increase in AUC, C<sub>max</sub>, and T<sub>max</sub> for the pravastatin metabolite SQ 31,906. Combination therapy with pravastatin and gemfibrozil is generally not recommended.

In interaction studies with aspirin, antacids (1 hour prior to PRAVACHOL), cimetidine, nicotinic acid, or probucol, no statistically significant differences in bioavailability were seen when PRAVACHOL (pravastatin sodium) was administered.

**Other Drugs:** During clinical trials, no noticeable drug interactions were reported when PRAVACHOL was added to: diuretics, antihypertensives, digitalis, converting-enzyme inhibitors, calcium channel blockers, beta-blockers, or nitroglycerin.

**Endocrine Function:** HMG-CoA reductase inhibitors interfere with cholesterol synthesis and lower circulating cholesterol levels and, as such, might theoretically blunt adrenal or gonadal steroid hormone production. Results of clinical trials with pravastatin in males and post-menopausal females were inconsistent with regard to possible effects of the drug on basal steroid hormone levels. In a study of 21 males, the mean testosterone response to human chorionic gonadotropin was significantly reduced (p<0.004) after 16 weeks of treatment with 40 mg of pravastatin. However, the percentage of patients showing a  $\geq$ 50% rise in plasma testosterone after human chorionic gonadotropin stimulation did not change significantly after therapy in these patients. The effects of HMG-CoA reductase inhibitors on spermatogenesis and fertility have not been studied in adequate numbers of patients. The effects, if any, of pravastatin on the pituitary-gonadal axis in pre-menopausal females are unknown. Patients treated with pravastatin who display clinical evidence of endocrine dysfunction should be evaluated appropriately. Caution should also be exercised if an HMG-CoA reductase inhibitor or other agent used to lower cholesterol levels is administered to patients also receiving other drugs (e.g., ketoconazole, spironolactone, cimetidine) that may diminish the levels or activity of steroid hormones.

**CNS Toxicity:** CNS vascular lesions, characterized by perivascular hemorrhage and edema and mononuclear cell infiltration of perivascular spaces, were seen in dogs treated with pravastatin at a dose of 25 mg/kg/day, a dose that produced a plasma drug level about 50 times higher than the mean drug level in humans taking 40 mg/day. Similar CNS vascular lesions have been observed with several other drugs in this class.

A chemically similar drug in this class produced optic nerve degeneration (Wallerian degeneration of retinogeniculate fibers) in clinically normal dogs in a dose-dependent fashion starting at 60 mg/kg/day, a dose that produced mean plasma drug levels about 30 times higher than the mean drug level in humans taking the highest recommended dose (as measured by total enzyme inhibitory activity). This same drug also produced vestibuloocular Wallerian-like degeneration and retinal ganglion cell chromatolysis in dogs treated for 14 weeks at 180 mg/kg/day, a dose which resulted in a mean plasma drug level similar to that seen with the 60 mg/kg dose.

**Carcinogenesis, Mutagenesis, Impairment of Fertility:** In a 2-year study in rats fed pravastatin at doses of 10, 30, or 100 mg/kg body weight, there was an increased incidence of hepatocellular carcinomas in males at the highest dose (p<0.01). Although rats were given up to 125 times the human dose (h<sub>TD</sub>) on a mg/kg body weight basis, their serum drug levels were only 6 to 10 times higher than those measured in humans given 40 mg pravastatin as measured by AUC.

The oral administration of 10, 30, or 100 mg/kg (producing plasma drug levels approximately 0.5 to 5.0 times human drug levels at 40 mg) of pravastatin to mice for 22 months resulted in a statistically significant increase in the incidence of malignant lymphomas in treated females when all treatment groups were pooled and compared to controls (p<0.05). The incidence was not dose-related and male mice were not affected.

A chemically similar drug in this class was administered to mice for 72 weeks at 25, 100, and 400 mg/kg body weight, which resulted in mean serum drug levels approximately 3, 15, and 33 times higher than the mean human serum drug concentration (as total inhibitory activity) after a 40 mg oral dose. Liver carcinomas were significantly increased in high-dose females and mid- and high-dose males, with a maximum incidence of 90 percent in males. The incidence of adenomas of the liver was significantly increased in mid- and high-dose females. Drug treatment also significantly increased the incidence of lung adenomas in mid- and high-dose males and females. Adenomas of the eye-Harderian gland (a gland of the eye of rodents) were significantly higher in high-dose mice than in controls.

No evidence of mutagenicity was observed *in vitro*, with or without rat-liver metabolic activation, in the following studies: microbial mutagen tests, using mutant strains of *Salmonella typhimurium* or *Escherichia coli*; a forward mutation assay in L5178Y TK +/– mouse lymphoma cells; a chromosomal aberration test in hamster cells; and a gene conversion assay using *Saccharomyces cerevisiae*. In addition, there was no evidence of mutagenicity in either a dominant lethal test in mice or a micronucleus test in mice.

In a study in rats, with daily doses up to 500 mg/kg, pravastatin did not produce any adverse effects on fertility or general reproductive performance. However, in a study with another HMG-CoA reductase inhibitor, there was decreased fertility in male rats treated for 34 weeks at 25 mg/kg body weight, although this effect was not observed in a subsequent fertility study when the same dose was administered for 11 weeks (the entire cycle of spermatogenesis, including epididymal maturation). In rats treated with this same reductase inhibitor at 180 mg/kg/day, seminiferous tubule degeneration (necrosis and loss of spermatogenic epithelium) was observed. Although not seen with pravastatin, two similar drugs in this class caused drug-related testicular atrophy, decreased spermatogenesis, spermatocytic degeneration, and giant cell formation in dogs. The clinical significance of these findings is unclear.

**Pregnancy: Pregnancy Category X:** See CONTRAINDICATIONS.

Safety in pregnant women has not been established. Pravastatin was not teratogenic in rats at doses up to 1000 mg/kg daily or in rabbits at doses of up to 50 mg/kg/day. These doses resulted in 20x (rabbit) or 240x (rat) the human exposure based on surface area (mg/meter<sup>2</sup>). However, in studies with another HMG-CoA reductase inhibitor, skeletal malformations were observed in rats and mice. PRAVACHOL (pravastatin sodium) should be administered to women of child-bearing potential only when such patients are highly unlikely to conceive and have been informed of the potential hazards. If the woman becomes pregnant while taking PRAVACHOL (pravastatin sodium), it should be discontinued and the patient advised again as to the potential hazards to the fetus.

**Nursing Mothers:** A small amount of pravastatin is excreted in human breast milk. Because of the potential for serious adverse reactions in nursing infants, women taking PRAVACHOL should not nurse (see CONTRAINDICATIONS).

**Pediatric Use:** Safety and effectiveness in individuals less than 18 years old have not been established. Hence, treatment in patients less than 18 years old is not recommended at this time. (See also PRECAUTIONS: General.)

**ADVERSE REACTIONS**

Pravastatin is generally well tolerated; adverse reactions have usually been mild and transient. In 4-month long placebo-controlled trials, 1.7% of pravastatin-treated patients and 1.2% of placebo-treated patients were discontinued from treatment because of adverse experiences attributed to study drug therapy; this difference was not statistically significant. In long-term studies, the most common reasons for discontinuation were asymptomatic serum transaminase increases and mild, non-specific gastrointestinal complaints. During clinical trials the overall incidence of adverse events in the elderly was not different from the incidence observed in younger patients.

**Adverse Clinical Events:** All adverse clinical events (regardless of attribution) reported in more than 2% of pravastatin-treated patients in the placebo-controlled trials are identified in the table below; also shown are the percentages of patients in whom these medical events were believed to be related or possibly related to the drug:

Body System/Event	All Events %		Events Attributed to Study Drug %	
	Pravastatin (N=900)	Placebo (N=411)	Pravastatin (N=900)	Placebo (N=411)
Cardiovascular				
Cardiac Chest Pain	4.0	3.4	0.1	0.0
Dermatologic				
Rash	4.0*	1.1	1.3	0.9
Gastrointestinal				
Nausea/Vomiting	7.3	7.1	2.9	3.4
Diarrhea	6.2	5.6	2.0	1.9
Abdominal Pain	5.4	6.9	2.0	3.9
Constipation	4.0	7.1	2.4	5.1
Flatulence	3.3	3.6	2.7	3.4
Hburtum	2.9	1.9	2.0	0.7
General				
Fatigue	3.8	3.4	1.9	1.0
Chest Pain	3.7	1.9	0.3	0.2
Influenza	2.4*	0.7	0.0	0.0
Musculoskeletal				
Localized Pain	10.0	9.0	1.4	1.5
Myalgia	2.7	1.0	0.6	0.0
Nervous System				
Headache	6.2	3.9	1.7*	0.2
Dizziness	3.3	3.2	1.0	0.5
Renal/Genitourinary				
Urinary Abnormality	2.4	2.9	0.7	1.2
Respiratory				
Common Cold	7.0	6.3	0.0	0.0
Rhinitis	4.0	4.1	0.1	0.0
Cough	2.6	1.7	0.1	0.0

\*Statistically significantly different from placebo.

The following effects have been reported with drugs in this class:

**Skeletal:** myopathy, rhabdomyolysis.

**Neurological:** dysfunction of certain cranial nerves (including alteration of taste, impairment of extra-ocular movement, facial paresis); tremor, vertigo, memory loss, paresthesia, peripheral neuropathy, peripheral nerve palsy.

**Sensitivity Reactions:** An apparent hypersensitivity syndrome has been reported rarely which has included one or more of the following features: anaphylaxis, angioedema, lupus erythematosus-like syndrome, polymyalgia rheumatica, vasculitis, purpura, thrombocytopenia, leukopenia, hemolytic anemia, positive ANA, ESR increase, arthritis, arthralgia, urticaria, asthenia, photosensitivity, fever, chills, flushing, malaise, dyspnea, toxic epidermal necrolysis, erythema multiforme, including Stevens-Johnson syndrome.

**Gastrointestinal:** pancreatitis, hepatitis, including chronic active hepatitis, cholestatic jaundice, fatty change in liver, and, rarely, cirrhosis, fulminant hepatic necrosis, and hepatoma; anorexia, vomiting.

**Reproductive:** gynecostasia, loss of libido, erectile dysfunction.

**Eye:** progression of cataracts (lens opacities), ophthalmoplegia.

**Laboratory Test Abnormalities:** Increases in serum transaminase (ALT, AST) values and CPK have been observed (see WARNINGS).

Transient, asymptomatic eosinophilia has been reported. Eosinophil counts usually returned to normal despite continued therapy. Anemia, thrombocytopenia, and leukopenia have been reported with other HMG-CoA reductase inhibitors.

**Concomitant Therapy:** Pravastatin has been administered concurrently with cholestyramine, colestipol, nicotinic acid, probucol and gemfibrozil. Preliminary data suggest that the addition of either probucol or gemfibrozil to therapy with lovastatin or pravastatin is not associated with greater reduction in LDL-cholesterol than that achieved with lovastatin or pravastatin alone. No adverse reactions unique to the combination or in addition to those previously reported for each drug alone have been reported. Myopathy and rhabdomyolysis (with or without acute renal failure) have been reported when another HMG-CoA reductase inhibitor was used in combination with immunosuppressive drugs, gemfibrozil, erythromycin, or lipid-lowering doses of nicotinic acid. Concomitant therapy with HMG-CoA reductase inhibitors and these agents is generally not recommended. (See WARNINGS: Skeletal Muscle and PRECAUTIONS: Drug Interactions.)

**OVERDOSAGE**

There have been no reports of overdoses with pravastatin. Should an accidental overdose occur, treat symptomatically and institute supportive measures as required.

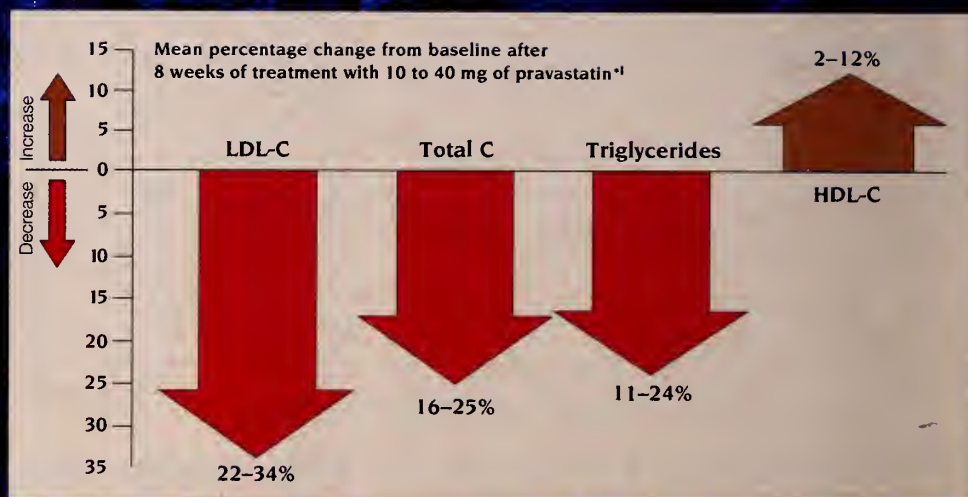






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\*Each arrow represents a range of means derived from a single placebo-controlled study that included 55 patients treated with pravastatin.

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**Reference:** 1. Jones PH, et al. Once-daily pravastatin in patients with primary hypercholesterolemia: a dose-response study. *Clin Cardiol.* 1991;14:146-151.

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Please see CONTRAINDICATIONS, WARNINGS, PRECAUTIONS, and ADVERSE REACTIONS in the brief summary of prescribing information on the adjacent page.



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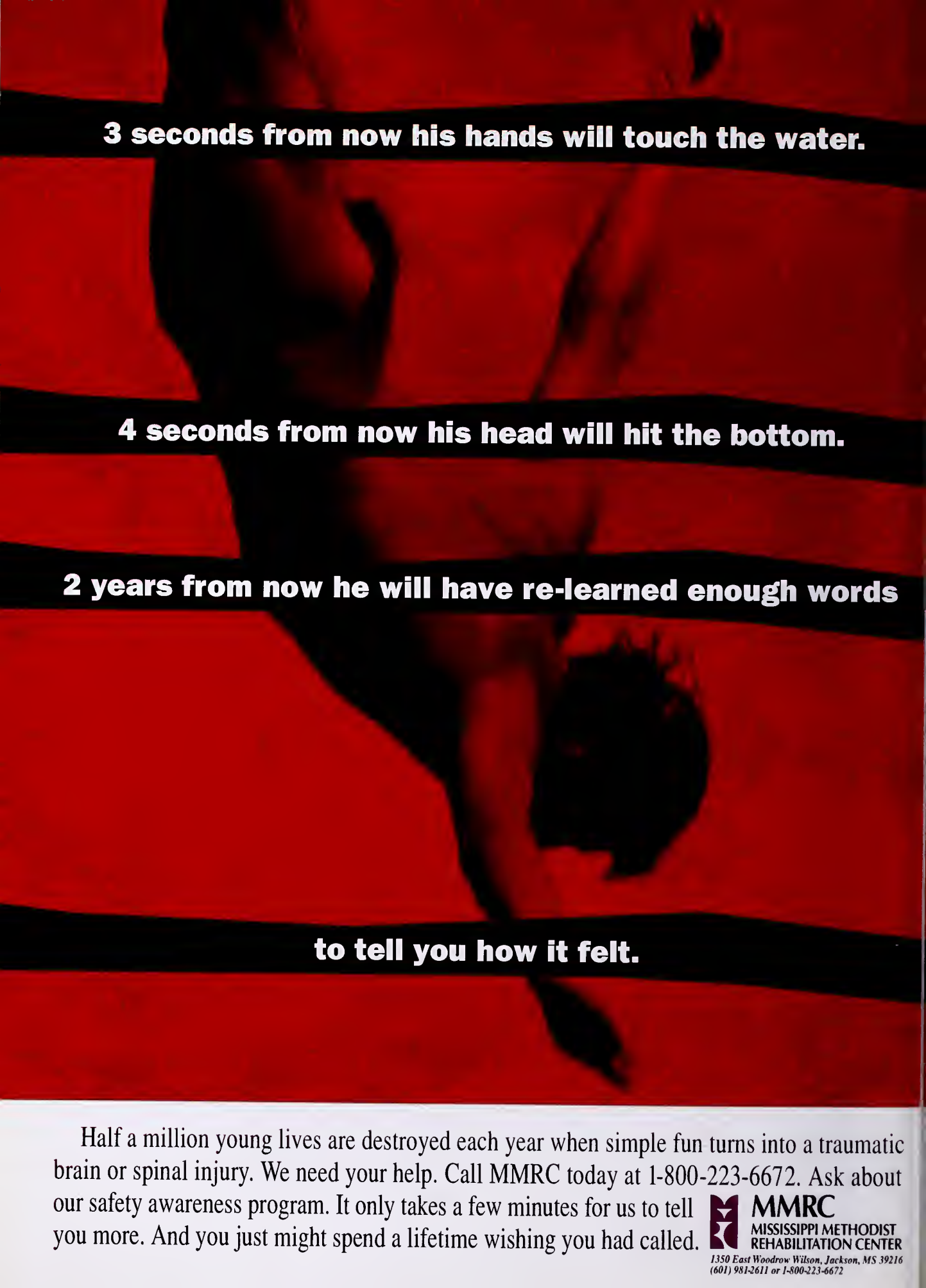
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OF THE MISSISSIPPI STATE MEDICAL ASSOCIATION

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VOLUME XXXIV

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## SCIENTIFIC ARTICLES

- Laparoscopic Colectomy For Sigmoid Volvulus** 73  
*Bruce Pruett, MD*
- The Effects Of Malpractice On Mississippi Physicians** 77  
*Alexis Polles, MD and Susan M. Neral, PhD*

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## SPECIAL ARTICLE

- Back Then - Plus Ten Commandments For Graduates With Illustrative Cases** 83  
*James D. Hardy, MD*

## EDITORIALS

- Gemütlichkeit** 86  
*William C. Gates, Jr., MD*
- Home Health Reimbursement** 87  
*George Abraham, MD, Associate Editor*

## DEPARTMENTS

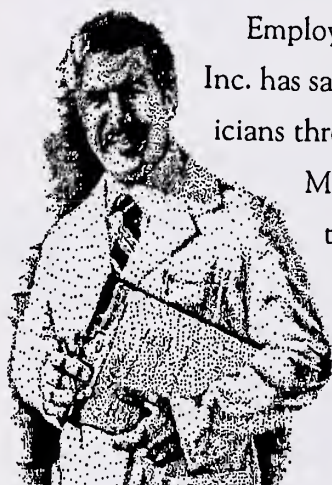
- Letters** 90
- Current Opinions** 93
- Medical Organization** 96
- 125th Annual Session Program Overview** 98
- Personals** 100
- Placement Service** 104

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# Laparoscopic Colectomy For Sigmoid Volvulus

BRUCE PRUETT, MD

With the recent explosion of laparoscopic techniques onto the general surgery scene, more procedures are being performed with minimally invasive access. Since the advent of new stapling instruments, laparoscopic bowel resections are now not only possible, but have already been safely performed in multiple centers. Laparoscopic colon resections are being performed for the same indications as a standard open laparotomy and colectomy, but with less morbidity.

Laparoscopic colectomy has many advantages; less pain, little or no ileus, a shorter hospitalization, quicker return to normal activity and a superior cosmetic appearance. Disadvantages of this procedure are inability to palpate the colon and 40 to 50% more anesthesia time.<sup>1-3</sup>

### Case Report

A 44 year old white male who was mentally retarded and had severe seizure disorder, pre-

Laparoscopic assisted sigmoidectomy was the technique of choice for a mentally retarded adult male with severe seizure disorder and recurrent sigmoid volvulus in an effort to reduce post-op stress and discomfort and thereby diminish the possibility of exacerbation of his seizures. The technique was performed using standard laparoscopic technique and a 5cm incision in the left abdomen to perform extracorporeal bowel anastomosis. The surgery was successful and the patient experienced minimal post op discomfort, no complications and had no seizures. This newest addition to the portfolio of laparoscopic surgical techniques may be a useful tool in high risk or elderly patients who are poor candidates for conventional bowel surgery.

sented with recurrent sigmoid volvulus. Approximately one year earlier, the patient had his initial episode of transient sigmoid volvulus that reduced with barium enema. On presentation to the Emergency Department on this hospital admission, the patient's sisters who are his care

givers, gave a history of severe chronic constipation, chronic abdominal distentions and severe pain.

Physical examination confirmed distention and tenderness of the abdomen. Abdominal xrays showed marked elongation of the colon with extensive gas-

eous distention extending down to the descending colon. There was a very prominent sigmoid loop projecting over into the right mid-abdomen. No free air was seen on xray.

The colon was so extremely dilated that the concern over impending perforation prompted urgent colonoscopic decompression and placement of a colorectal decompression tube. The patient tolerated this well. There was good relief of the volvulus and good decompression of the colonic distention. However, as soon as the tube was removed the sigmoid volvulus recurred and colonoscopic decompression was once again used.

The patient's family was very reluctant to consider laparotomy and sigmoid resection because they believed the post-op stress and pain would make his refractory seizure disorder unmanageable. After discussion of their concerns, laparoscopically assisted colon resection was suggested as a means of correcting the problem of the megacolon and sigmoid volvulus without making the patient endure a large painful laparotomy incision. After the details of the technique and the risks and benefits were carefully explained, the family decided to proceed with laparoscopic sigmoid colon resection.

The patient was prepared for surgery with a Colyte oral prep and both oral and parenteral antibiotics. In the operative suite the patient was positioned supine. Under general anesthesia a nasogastric tube and a urinary catheter were inserted. The abdomen was widely prepped and draped. After placing a Verres needle through the right mid abdomen, carbon dioxide was insufflated to 14 mm Hg pressure. A 10 mm laparoscopic trocar and cannula was then in-

serted and the 10 mm laparoscope placed into the peritoneal cavity. Under laparoscopic vision the remaining laparoscopic trocars were placed in the left upper and lower quadrants, and right upper and lower quadrants. The sigmoid colon was grasped with Babcock graspers and elevated. The mesentery at the rectosigmoid was dissected with cautery scissors, thereby opening a small window in the mesentery. The Endo GIA 3.5 stapler was inserted and used to transect the rectosigmoid junction by firing the stapler three consecutive times using the multi-fire instrument.

At this point, the proximal extent of the colon resection was determined and the colon transected in the same manner using the Multi-fire Endo GIA. The mesentery was then divided using the hand held suction cautery and Endoclips on the smaller vessels and the vascular Endo GIA stapler at the base of the mesentery for the larger vessels.

Once the sigmoid colon and its mesentery were unattached and free in the abdomen, a small transverse incision, 5 centimeters in length was made in the left abdomen. The resected sigmoid colon and mesentery were removed and the proximal and distal colon ends were handed out through the incision. A side-to-side GIA stapled anastomosis was performed and closed with a TA 55. The completed anastomosis was inspected and then dropped back into the abdomen. The peritoneum, fascia and skin were closed. The subcutaneous fat was drained with a penrose drain. The abdomen was then reinsufflated, inspected, and irrigated with saline and suctioned clear of fluid. The laparoscopic instruments were then removed,

the carbon dioxide evacuated, the puncture incisions closed and all wounds injected with Marcaine local anesthetic.

The patient's post-op course was unremarkable. He had no refractory seizures, experienced minimal discomfort, and had no post op complications. On post operative visit to the office his family reported resolution of abdominal distention and constipation.

## Discussion

It is predicted that within five years 70% of all colectomies will be laparoscopic.<sup>1</sup> The laparoscopic assisted colectomy may be a useful alternative in high risk patients or in the elderly who may not tolerate conventional colon surgery. The ideal candidate is not obese, has not had multiple abdominal surgery, and requires a right colon or sigmoid resection which is less tedious to perform with a laparoscopic approach than the flexures, transverse colon or rectum.<sup>1</sup> Small incisions, 4-8cms, used to remove specimens, can also be used to perform extracorporeal anastomosis, if the remaining bowel lengths are sufficient, thereby combining open and laparoscopic surgery techniques to their greatest benefit, while reducing post operative pain, ileus and recovery time over that of the conventional open technique.<sup>2</sup> Because the expected advantages, from the patient's perspective, far outweigh the downside, laparoscopic colectomy promises to be as popular and consumer driven as has been laparoscopic cholecystectomy. □

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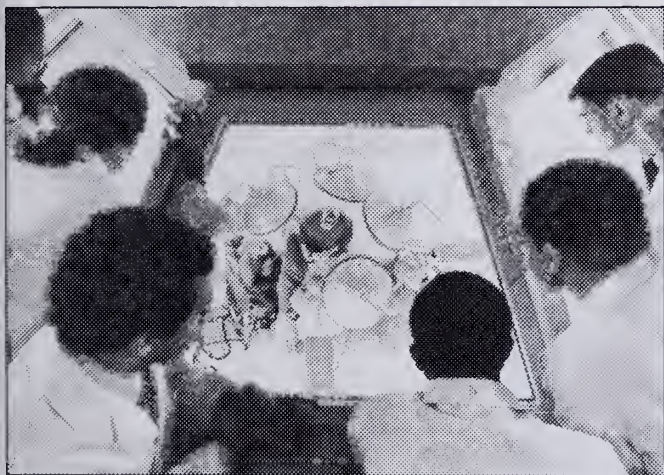
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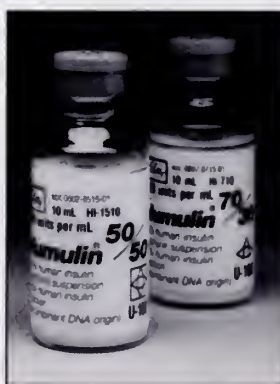
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# The Effects of Malpractice On Mississippi Physicians

ALEXIS POLLES, MD  
SUSAN M. NERAL, PhD

Medical malpractice and its effects on physicians in Mississippi is reviewed to assess its effects upon decisions in practice, patient care, and the physical and emotional toll on physicians. Through a random survey of 500 physicians in Mississippi across all areas of medicine it was determined that 47.3% of the respondents had been involved in malpractice litigation, a higher percentage than the United States average in 1989. The predominant emotional response to litigation was anger. Most physicians did not seek outside help as an aid in coping.

It is nearly impossible to go through a single day in checking through the mail or professional magazines and journals without seeing some information regarding risk management and malpractice. Professional liability suits are discussed as an expected occurrence with medical students and residents. It would be the rare physician who did not experience even slight discomfort at the mention of the term "malpractice". The discomfort seems justified. Indeed, among obstetricians and gynecologists in their national survey (The American College of Obstetricians and Gynecologists) in 1987, 70% had experienced at least one malpractice claim. This was verified by Begnaud at the same levels in our neighboring state of Louisiana in 1988.<sup>1</sup> The AMA Center for Health Policy

Research confirmed that as of 1989, nearly 40% of all physicians had had at least one claim during their careers.<sup>2</sup>

People may define malpractice in terms relevant to their own situation; however, there are definite legal criteria that define it. Malpractice is within the realm of medical negligence. The patient who becomes the plaintiff must through their legal counsel establish what has become known as the "4 D's":<sup>3</sup>

1. That a doctor-patient relationship existed, creating a duty to care.
2. That a doctor *deviated* from (breached) the duty of care by an act or omission not in accord with professional standards.
3. That the patient was *damaged* (harmed).
4. That the harm to the pa-

tient was *directly* (proximally) caused by the doctor's breach of duty.

These must be established by the plaintiff by a preponderance (>50 out of 100 chance) of evidence.

Actions that may create and be defined as a doctor-patient relationship:<sup>4</sup>

1. Giving advice.
2. Making interpretations.
3. Writing a prescription.
4. Supervising treatment by nonmedical personnel.
5. Holding lengthy phone conversations with a prospective patient.
6. Treating an unseen patient by mail.
7. Giving a patient an appointment.
8. Telling a walk-in patient that he or she will be seen.



9. Providing sample medications.
10. Acting as a substitute doctor.
11. Providing treatment during an evaluation.
12. Providing opinions to neighbors and friends.

Obviously, one of the areas of concern in malpractice involves money. For example, what happens to the money paid to companies in insurance premiums? According to Begneaud, only 28 cents of every insurance premium dollar goes to the malpractice victim. The remaining 72 cents goes to the plaintiff and defense attorneys and to the support of the legal and insurance industries.<sup>5</sup>

The monetary toll is only one aspect to consider in the price that malpractice claims exact. This study will review the data regarding financial, physical, medical and emotional costs for both patient and physician. Information provided by our colleagues in Mississippi regarding the effects of malpractice on the physician will be presented.

As a background for reporting the results of this survey, let us review some general facts about malpractice. Data regarding the frequency of claims and suits was taken from the two largest liability insurers in Mississippi - namely Medical Assurance Co. and The St. Paul Co. The number of claims peaked in 1985 and gradually declined until 1989.<sup>6</sup> The average costs of all reported claims countrywide is \$36,416. In years past, 2/3 of claims involving physicians occurred in the hospital setting, but recent data show increased claims being filed on services provided in office or clinic settings. Jury verdict research shows that the average award for medical liability has been con-

tinuously increasing.<sup>7</sup> The average rate of annual medical liability premiums in 1991 for \$1 mil/3 mil limits ranged from \$6,000 in Arkansas to about \$54,000 in Los Angeles. In Mississippi the average was \$13,874.<sup>8</sup>

Patients and physicians have been impacted in other ways. In Louisiana 85% of the surveyed participants said they had made some change in their practice in response to the malpractice risk. These changes included 77% who had raised their fees because of insurance premiums, 41% who had stopped treating indigent patients and 57% who were ordering more diagnostic studies.<sup>9</sup>

In a self-report survey of physicians who had been sued in the Chicago area published in 1984, 61.8% of the respondents ordered diagnostic tests even when they felt the tests were clinically unnecessary. Approximately 42% stopped seeing certain kinds of patients.<sup>10</sup> In a follow-up survey of both sued and non-sued physicians in the Chicago area published in 1985, both sued and non-sued physicians ordered more diagnostic tests and stopped performing high risk procedures. Nearly 50% of the sued physicians stopped seeing patients who they felt were more likely to present a risk for litigation.<sup>11</sup> Though these physicians may avoid Medicaid patients in order to reduce the exposure to possible litigation, a study done in Maryland revealed that Medicaid recipients were not more likely to file malpractice claims than people with other payment sources.<sup>12</sup>

The concern over malpractice risk appears to be the primary factor governing treatment decisions in some situations. A nationwide random sample of criti-

cal care physicians and physician members of the American Society of Law and Medicine were questioned about a hypothetical case. The scenario was a ventilator supported chronically comatose patient with unknown preferences about life support. The results showed that the importance ratings for physician legal liability best predicted management choices in the case.<sup>13</sup>

Malpractice litigation may also affect access to specialty and subspecialty services for some patient populations. In a survey of 293 physicians in 5 specialties, in a non-emergency situation, less than 20% of the respondents said they would treat a patient who had filed a suit against them, even if there were no alternative care available in the local area.<sup>14</sup> Not only would the access to specialty services, especially in small communities, be greatly reduced, but these physicians may be exposing themselves to additional legal action on charges of abandonment. Thus, it should be remembered that although either the physician or the patient can unilaterally terminate the relationship in a nonemergency setting, the physician must at least provide a list of potential referral physicians.<sup>15</sup>

Even though malpractice litigation may have the overall effects of improving medical care and giving compensation for patient injury in many instances, it has other disadvantages. Litigation apparently produces anger and anxiety in physicians, which exerts an adverse influence not only on the physician but also ultimately on the patient.<sup>16</sup> In the Chicago area physician surveys mentioned previously, there were two symptom clusters which emerged in the physi-

cians. These symptom clusters tended to be of worse severity in sued versus nonsued physicians though present in both. The first cluster included those with dysphoric mood with at least four more symptoms characteristic of an affective disorder (which might be comparable to a major depressive disorder). The second symptom cluster included those with significant anger associated with at least four of the following: depressed mood, inner tension, frustration, irritability, fatigue, gastrointestinal symptoms, or headache. About 6% of the respondents had onset of physical illness and half of these had been sued. Almost 10% had exacerbation of an existing illness. Three physicians suffered myocardial infarction which they related to the stress associated with the medical malpractice problem.<sup>17</sup>

From the same survey it is noteworthy that less than 2% of the sued respondents had actually received adverse trial verdicts. The chronic stress on both sued and nonsued physicians appears to be detrimental to the quality and availability of medical care. The ultimate outcome of the claim also appears to be a relatively minor stressor when compared with the chronic stress of the process.<sup>18</sup>

### **Rationale**

Information gleaned from studies like the Chicago survey are not generalizable because the physicians responding were in a large urban area. The current survey we carried out sought information from our own backyard. We surveyed Mississippi physicians to see how this so-called crisis has affected them, and to see if the experience of physicians in a largely rural

state is similar to that of physicians in a densely populated urban center.

### **Methodology**

Information was received by way of responses to a mailout survey form which consisted of 37 questions with forced-choice answers.

The questionnaire was designed by the principal investigators to cover six broad areas:

1. Malpractice Claims.
2. Effects on Practice.
3. Effects on Self.
4. Effects on Other Relationships.
5. Biographical Data.
6. Subsequent and/or Future Suits.

The sample population consisted of 500 randomly selected physicians who hold Mississippi licenses in all areas of medicine listed by the Mississippi State Medical Association.

The survey envelope contained a cover letter, questionnaire, and return envelope. Only one mail-out was initiated. The overall usable response rate was 44.5% or 222 of the 500 questionnaires mailed.

### **Results**

Responses in the survey regarding effects of malpractice litigation were limited to physicians who had actually been involved directly in litigation. The results of the 222 questionnaires were analyzed and the following data were revealed. Although 224 questionnaires were returned, 2 of the respondents did not indicate whether or not they had ever been sued and those results were not included. The consistency of responses was not uniform, meaning that respondents seemed to answer selected questions throughout the questionnaire and to leave others blank.

Initial statistical analysis yielded descriptive frequency data that were computed on all 222 respondents (these will be reported in raw numbers). The remaining descriptive data were gleaned from the initial analysis by computing percentages based on the number of individuals who completed their response on any given variable (these will be reported in percentages).

Considering general demographic information, of all 224 who returned the questionnaire, chronological ages ranged from 24-80, the mean age being 46.9 and the median being 47. Of all respondents, both sued and nonsued, a significant 93% were married, and the remaining 7% were: 3% single, 2% divorced, and 2% widowed.

Another demographic variable considered was the primary area of practice. The top eight specialty areas represented were family practice with 43, internal medicine with 20, general surgery with 18, OB-GYN with 15, radiology with 13, orthopedic surgery with 13, ENT with 12 and pediatrics with 11.

The next variable considered was number of years in practice. 12% of all respondents had been in practice < 5 years, 19% from 5-10 years, 32% from 10-20 years, and 35% > 20 years. In follow-up analysis there was no correlation between years of practice and likelihood of a suit.

Considering demographics again, as far as types of practice, 52% were in group practices with 39% in solo practices. The data regarding institutional practice could not be accurately analyzed because responses were inconsistent. Considering the location of practices, of the sued and nonsued physicians, 71% were in what was called an urban practice (which was defined as a



population >15,000). It is important to consider, however, that the perception of urban communities in the state of Mississippi may differ significantly from perception in other areas of the country.

This concludes the analysis of demographics. The preceding demographic data and the following findings related to anxiety included sued and non-sued respondents. Of physicians who responded, 48% indicated that reporting of malpractice litigation settlements in the Physicians' Data Bank has increased their anxiety.

When asked to consider the risk of malpractice, 36% of all respondents, indicated that they thought they were at greater risk of malpractice in Mississippi than in other southeastern states. Although this information was not available on a state-by-state basis, it is general knowledge that Florida physicians are at greatest risk among all southeastern states.

Of all respondents, 47.3% indicated that they had been involved in malpractice litigation, which is higher than the 40% U.S. average in 1989 mentioned earlier.<sup>19</sup> Of those who have ever been involved, 23% were currently under litigation.

In reporting their opinion of the outcome of those cases which had been settled, 61% of the participants felt that a satisfactory solution had been found. On the other hand, 34% of respondents indicated that the outcome was either ridiculous (19%) or very unfair (15%).

It is noteworthy that 60% of those who responded to this question indicated that their case was either dropped without action (27%) or settled out of court (33%). The predominant emotional response to being sued

was anger, with 89 respondents admitting to this. This response may correspond to the pervasive anger symptom cluster described in the results of the Chicago survey.<sup>20</sup>

More impressive, however, are the additional comments written in by some of the respondents. One respondent who had been sued more than fifteen years ago (at the age of 31) endorsed feeling angry, having financial fears, and experiencing depression. He states "my worst problem was the three years from the time the suit was filed until it was settled. Also, my insurance carrier's lawyer was very rude and unsupportive. He had a very low opinion of doctors and was verbally abusive at times". Another physician wrote, "this really kicks the wind out of a practicing physician, especially when the question of malpractice is questionable". The emotional response of 88% of the participants did not include wishes to harm themselves or others.

The next series of questions involved sources of support. Eighty-one respondents indicated that they received support from their family, 52 indicated support from friends, 58 from colleagues, and 41 received support from office staff. On this question more than one source of support could be indicated.

Of those who had been sued, a surprising 96% did not seek professional help as a source of support. Even when asked to think retrospectively, an again surprising 89.5% felt that seeking support from others would not have been helpful or were unsure as to whether it would have helped. One respondent added comments that he or she did not need support and that he/she "went on with life - we are not all dependent morons". This

same respondent also perceived his risk of having a suit filed in the next ten years as 100%.

Other than direct effects on clinical treatment or cases, the next series of questions focused on the effects on relationship issues. Results revealed that 82 respondents indicated they did not perceive a change in family relationships, 83 of the respondents indicated that there was no change in relationships with colleagues, 8 respondents reported no change with office staff relations, and 94 reported no change with hospital staff.

On a question regarding coping mechanisms that included the use of alcohol, benzodiazepines, and other drugs including antidepressants, eating, and exercise, > 95% of respondents did not answer any items at all. Three respondents, however, did admit that they had self prescribed benzodiazepines or antidepressants. This is in contrast to a 1992 survey of U.S. physicians in which, 1 of every 9 physicians had self-prescribed and administered benzodiazepines or minor opiates in the preceding year.<sup>21</sup> There is certainly a possibility that this unsupervised self treatment with controlled substances could increase the risk for substance abuse or dependence. In the same survey, 8% of physicians admitted that they had experienced substance abuse or dependence.<sup>22</sup> These responses probably leave out a significant number who have not yet recognized that they have a problem.

## Conclusions

Based on the findings of this survey, Mississippi had a higher rate of malpractice litigation than that of the U.S. in general.<sup>23</sup> The majority of those who had been involved in litigation were satisfied with the outcome of the



case. Mississippi physicians reported anger as their primary emotional response. Family members provided the most common source of support for the physicians.

It is through participation in responding to questionnaires such as this that we can begin to assess the cost vs benefit to all those involved in such important issues in medicine. Hopefully, this will help us all to be able to make better decisions and choices in the difficult times facing us all in providing quality health care.

### Closing Statement

Finally, the comments of one of the respondents seemed to best summarize the dilemma for physicians. "Physicians are human beings and consequently subject to error. Physicians are required to make hundreds and perhaps thousands of decisions daily. Obviously they cannot all be correct. No physician can practice medicine for 15-20 years without making an occasional error. A few of these we can look back on and wonder how we could be so stupid or so negligent!"

"Conversely, we get credit for cures [for which] we had very little to contribute to nature's healing. We also get blamed for bad results when no human being could have done better. The unwarranted credit and [the] blame must all be kept in proper perspective."□

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## Special Article

# Back Then - Plus Ten Commandments For Graduates With Illustrative Cases

JAMES D. HARDY, MD, FACS

*Presented at University of Pennsylvania Medical School Commencement, Philadelphia, May 28, 1992*

**I**t is a signal honor, and a unique privilege, to welcome the class of 1992, on behalf of our class of 1942. And it has been grand to be here at Penn with our class this weekend.

When in 1884 Louis Pasteur addressed the medical students at the University of Edinburgh, he looked up to them and said, "Great things. You have indeed seen them."\*

And our class of '42 has indeed seen them: the advent of antibiotics, isotopes, control of poliomyelitis and other infectious diseases, renal dialysis, long-term endotracheal support, moni-

toring of blood gases and intraarterial pressures, computers (begun at Penn) and laboratory automation; arteriography, sonography, CT, MRI and PET imaging; cardiovascular surgery and transplantation; and a host of other advances. In sum, like the tide that lifts all ships, the prodigious progress in the basic sciences has made possible major advances in every clinical discipline. But for all this, my most poignant memory goes back to a young student nurse who developed rheumatic fever. She was put at bed rest in a private room on Maloney private floor. (The University Hospital took good care of its people.) Within weeks she had developed the opening snap of mitral stenosis. Surgery

for mitral stenosis was yet to come, and the mortality rate for subacute bacterial endocarditis then was almost that of AIDS today.

I will now complete my remarks by offering ten suggestions, or ten commandments, as it were - to the graduates. Fifty years from now you can look back and decide which of these you had found to be operative.

### **I. First: Honor thy Faculty and Administration.**

It is they who have established the worldwide prestige of the diploma which you are about to receive.

### **II. Second: Always Remember Who You Are and What You Represent.**

Within the hour you will be-

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\* Vallery-Radot, Rene, *The Life of Pasteur*, Garden City Publishing Co., Inc., Garden City, NY.



come "The Doctor," and your lives and relationships with others will be subtly changed forever.

*An Illustrative Case.* Recently a young female physician of my close acquaintance, a gastroenterologist, was startled and in fact acutely offended that a male in-law by her marriage had asked her about his very private and sensitive health problem. However, as a *physician*, she might have been gratified that he felt he *could* ask her, *The Doctor*.

The reverse of this, I can tell you, is to have a recent female graduate perform a ruthlessly complete insurance physical examination on her former Chairman of Surgery!

### **III. Third: Continue to Improve Work Habits, Efficiency and Excellence.**

You are constantly observed for larger responsibilities.

*An Illustrative Case.* When I was a surgical resident here, I came upon a chart which reflected a superb history and physical examination, and Dr. Ravdin, Chairman of Surgery, agreed that we should try to recruit this rotating intern for surgery. (All the internships were "rotating" at that time.) He chose medicine, though, and went on to a very distinguished career. But note the universal admiration for a good history and physical examination.

*"Each Job is a portrait of the person who did it."*

### **IV. Fourth: Educational and Professional Growth Must Be Continued Throughout A Career.**

*An Illustrative Case.* An early middle-aged surgeon, once well-trained at a major clinic, made an appointment with me. He had not kept up, as new surgical techniques and operations had come

along over the years, and now his practice had dwindled to below the make-ends-meet level. He borrowed money, uprooted his family, took oncology training in New York, and later became successful in Florida.

In addition to your own specialty journals, you should also enjoy the cultural value of general medical progress, as reflected in the New England Journal of Medicine and the JAMA. Books are also important but they should always be returned, even if late. For example, *after 50 years*, I recently returned to John Gislason, classmate and internship roommate, his freshman anatomy book. He thanked me for returning the book, but he failed to thank me for having transformed a second-hand Cunningham's Anatomy into a medical history book of true value!

### **V. Fifth: Treasure and Preserve Your Clinical Integrity.**

*An Illustrative Case.* An internist in Jackson, a Penn graduate, insisted he could get practically any patient operated upon; that if he truly wanted a surgical opinion, he called surgeon A, who might or might not agree to surgery. But if he simply wanted the patient operated upon, no questions asked, he called Dr. A's partner, Surgeon B. And I suspected that the internist was right.

One's clinical reputation is built case by case, day by day and morality is the ultimate reality.

### **VI. Sixth: Prepare For Leadership.**

A graduate of Pennsylvania is expected - in fact, obligated - to accept leadership roles in medicine. Fortunately, one can prepare for these future responsibilities by consistent reading, by

presenting material at staff meetings, and by writing up case reports for appropriate journals.

But I must confess that my own attempts to train our medical students in public speaking weren't always tranquil.

*An Illustrative Case.* I had passed out review slips, each bearing a surgical condition that the recipient was to arise and discuss for two minutes. When a female student heatedly refused, I declared that I could discuss *anything* for two minutes. Instantly, she snapped, "Discuss baroque art!" Momentarily taken back, I substituted the French Impressionists.

Before leaving Commandment Six, I must stress the importance of loyalty - in all its dimensions and directions - in achieving effective leadership.

### **VII. Seventh: Admire and Nourish Professional Relationships.**

In the course of a busy day during internship or residency or later in practice, it can be all too easy not to answer a consultation, or not to return telephone calls, or to talk down to the outside physician who seeks to send a patient, or to suggest publicly that such and such a patient was treated inappropriately. But professional courtesy is golden.

*An Illustrative Case.* A few weeks ago a physician called me, sick at heart. His beloved wife, a heavy smoker, had recently died of oat cell carcinoma. No chest x-rays for years. He blamed himself. But he also felt great bitterness that only two of the 28 physicians who treated her illness had ever called her by name. And several had even discussed the terminal resuscitation policy at the bedside, in her conscious hearing.

"Do unto others...."

### **VIII. Eighth: On Achiev-**

**ing Immortality.**

Great teachers live on. Dr. O. H. Perry Pepper, Professor of Medicine, showed us a patient our freshman year and then brought another patient with the same condition four years later to his last class with us. He asked if anyone remembered the diagnosis. As one, the class thundered, "Herpes zoster ophthalmicus."

Immortality has many forms and dimensions, but at least some of these are available to every physician: whether with patients, family, students, scientific contributions and so forth.

But I refer here to teaching - not necessarily of medical students and residents, but of nurses, technicians, office staff, physician colleagues and the public at large. Patience is important in teaching.

*An Illustrative Case.* One night about twenty-five years ago we were operating for a ruptured aortic aneurysm. The anesthesiologists were madly pumping blood, and I was trying to reduce blood loss and to clamp the aorta. Exhorting the assistants to still greater effort, I had apparently said vehemently, "There's not an operator in a carload of you fellows." Well, that chief resident, for many years now a richly successful cardiovascular surgeon, still remembers my comment.

Sticks and stones can break the bones, but *words* can break the *heart*. Most mammals do better with approval.

**IX. Ninth: Nurture Your Family.**

Plan for, and spend time alone with, each child. They will never forget it, and it will be the best investment you'll ever make. And remember, the greatest thing a parent can do for the children is to love the spouse.

Strong and healthy children

are important to our medical profession. Our registrar tells me that children of physicians represent from 10% to 15% of each medical class.


Lastly, take quiet time, alone with silence, for yourself - for creative thinking or just for thinking things through. And always keep a notebook at hand to capture useful thoughts.

**X. Tenth: Enjoy your work.** You have earned that very special privilege of having a secure and splendid job for the rest of your lives. There is nothing more sustaining, throughout the vicissitudes of life, than the daily pursuit of important work

that you truly enjoy.

In closing, we wish you, the '92 graduates, every success and happiness in your challenging internship-residencies and forever thereafter. We, the class of 1942, now pass the baton to *you*, for *your* fifty years. We've had a marvelous time in medicine. We have seen great things, and you will see great things. And we wish you well. □

*Dr. Hardy is Professor Emeritus, Department of Surgery, University of Mississippi Medical Center, Jackson, MS.*



"Ron's Rule — I give myself one week to meet new people and start having fun on a locum tenens assignment. It hasn't failed me yet."

Ron Richmond, MD, joined the CompHealth locum tenens medical staff when he completed his residency. He wanted to travel. He loves to meet people. A little time off sounded really good. And he thinks being exposed to different types of medical practice will serve him well when he returns to his hometown to establish a community health center.

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## The President's Page

WILLIAM C. GATES, MD

### GEMÜTLICHKEIT

**T**he title of this piece is a German word for something or a situation that is quite "comfortable" or "warm and cozy" like your favorite old shoes or a very pleasant visit with good friends or family. Another meaning is that of "indicating a general sense of well-being."

I think and I'll bet you do, too, that the feeling of *gemütlichkeit* is totally antithetic in describing the situation in which we now find ourselves as physicians in America today. In fact, doctors in the USA appear to be caught up in a state of high anxiety ... free-floating anxiety that fuels free-floating and indiscriminate hostility.

This fearsome and frustrating anxiety can be traced back to the myriad uncertainties created by the prospect of radical change in our health care delivery system and the inability to predict its impact on quality, access, autonomy and economy.

Some physicians cannot seem to bear even the idea of incremental change, much less the concept of total system reform. The emotional energy produced by the anxiety has once again (remember the "end of medicine" in the 60's when Medicare and Medicaid came into being?) created a situation where those in organized medicine are engaging in divisive dialogue and activities - "pot-shotting" each other to the delight of our detractors - when we should be in a mode of uniting our forces and rallying around the flags of patient and physician advocacy.

Our only real power lies in the commitment to our ideals - our "special interests" - the values that made us seek out medicine as our life's work in the first place. The commonality of what's right for our patients and the concern for our patients' welfare is the strength of our profession. It will serve us well and see us through these troubling times of change.

Let's look at change for a moment ... prismatically and analytically and see what we are up against.

All things change. All people change. Change is an inevitable consequence of living. All change is not bad, although there is an inherent inertia in every human being that

(Continued on page 87)



## Home Health Reimbursement

It is note-worthy that the Mississippi State Medical Association is now actively investigating the issue of physician reimbursement for management of home health services. This is an issue whose positive resolution is long overdue. The services provided by physicians, presently unreimbursed, are not trivial, as we are all aware. These services include (but are not limited to): 1) the review, verification, and approval of the patient care plan on a monthly basis, 2) the overall responsibility for the consequences of the implementation of that plan, 3) the fielding of day to day communications from the home health agency regarding problems with the patient or the care plan, and 4) ultimate responsibility for the cost incurred (since no care can be rendered without physician approval).

Some may say that payment for such services is covered by physician office fees. I am unaware of any rational increase in physician office fees which were made for that dedicated purpose, and such an argument seems ludicrous.

It is high time that MSMA and the AMA take an active role in promoting reasonable physician reimbursement for services rendered in the home care setting.

**George E. Abraham, II, MD**  
Associate Editor

## President's Page

(Continued from page 86)

seems to seek a path of resistance to change. The French have a saying, "*le plus ce change, le plus c'est le même chose ...*" (the more the change, the more it's the same). I think what they are saying is that change tends over time to go full circle ("What goes around comes around") and tends to seek some former equilibrium or status quo.

The trend to return to a prior status quo seems less likely nowadays since the very nature of change itself has changed - that is to say that the rate and substance of change is more rapid, multidirectional and global but not always predictable as in the past. We used to be able to predict trends as a consequence of change. The ability to predict changing trends was accurate enough to be used with success as a tool of management. We can no longer "manage change" but rather can only manage *through* change.

Why are the changes we are experiencing so profound and so powerful as pertains to the medical profession?

In the language of the new age, the futurists and social commentators have designated the changing of the rules, the lines on the field and the name of the game as "paradigm shift."

Paradigm shift is a fancy expression that says the

(Continued on page 88)

The editorial opinions expressed in this Journal are those of the indicated author. Editorial opinions are not expressions of the views, or official policies of The Mississippi State Medical Association. We encourage the membership to submit letters for publication regarding any opinion expressed or information contained in the Journal.

## President's Page

(Continued from page 87)

buoys and markers that we used to steer by and the very foundations that supported our behavior in many arenas are all changing in a deep, structural sense in society. Things are going to be different.

Paradigm shift is what sent politics as usual packing in the last election. Paradigm shift is what has created the upheavals we've seen in big business such as IBM, Sears, GM and GE. Paradigm shift is responsible for "down-sizing" in the military. Paradigm shift has medicine in its grip and that's the engine of change.

We physicians cannot effectively face the paradigm shift, the anxiety of inevitable change and the final products of change individually-all alone. No one of us is as strong as all of us and *never* has the need for unity of mind and purpose been stronger. We should remind each other, the public and the President that without the input of organized medicine there can be no meaningful reform of the health care system. We must send a unified message from medicine that the pressure to provide what fiscal planners *want* doesn't distract the policy-makers from what our patients *need*.

President Clinton said on his day of inauguration that there is nothing wrong with America that can't be fixed by what's right with America. We should remind him in every way possible that there is nothing wrong with America's health care system that can't be cured by what is good in American medicine. That can be our battle cry and the source of renewal of our *gemütlichkeit*.

I hope my note finds you and yours doing well....

Bill

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**Action:** Yohimbine blocks presynaptic alpha-2 adrenergic receptors. Its action on peripheral blood vessels resembles that of reserpine, though it is weaker and of short duration. Yohimbine's peripheral autonomic nervous system effect is to increase parasympathetic (cholinergic) and decrease sympathetic (adrenergic) activity. It is to be noted that in male sexual performance, erection is linked to cholinergic activity and to alpha-2 adrenergic blockade which may theoretically result in increased penile inflow, decreased penile outflow or both.

Yohimbine exerts a stimulating action on the mood and may increase anxiety. Such actions have not been adequately studied or related to dosage although they appear to require high doses of the drug. Yohimbine has a mild anti-diuretic action, probably via stimulation of hypothalamic centers and release of posterior pituitary hormone.

Reportedly, Yohimbine exerts no significant influence on cardiac stimulation and other effects mediated by B-adrenergic receptors, its effect on blood pressure, if any, would be to lower it; however no adequate studies are at hand to quantitate this effect in terms of Yohimbine dosage.

**Indications:** Yocon<sup>®</sup> is indicated as a sympathicolytic and mydriatic. It may have activity as an aphrodisiac.

**Contraindications:** Renal diseases, and patient's sensitive to the drug. In view of the limited and inadequate information at hand, no precise tabulation can be offered of additional contraindications.

**Warning:** Generally, this drug is not proposed for use in females and certainly must not be used during pregnancy. Neither is this drug proposed for use in pediatric, geriatric or cardio-renal patients with gastric or duodenal ulcer history. Nor should it be used in conjunction with mood-modifying drugs such as antidepressants, or in psychiatric patients in general.

**Adverse Reactions:** Yohimbine readily penetrates the (CNS) and produces a complex pattern of responses in lower doses than required to produce peripheral a-adrenergic blockade. These include, anti-diuresis, a general picture of central excitation including elevation of blood pressure and heart rate, increased motor activity, irritability and tremor. Sweating, nausea and vomiting are common after parenteral administration of the drug.<sup>1,2</sup> Also dizziness, headache, skin flushing reported when used orally.<sup>1,3</sup>

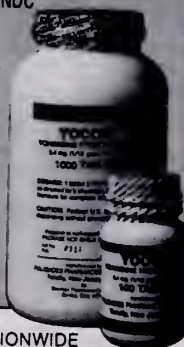
**Dosage and Administration:** Experimental dosage reported in treatment of erectile impotence.<sup>1,3,4</sup> 1 tablet (5.4 mg) 3 times a day, to adult males taken orally. Occasional side effects reported with this dosage are nausea, dizziness or nervousness. In the event of side effects dosage to be reduced to 1/2 tablet 3 times a day, followed by gradual increases to 1 tablet 3 times a day. Reported therapy not more than 10 weeks.<sup>3</sup>

**How Supplied:** Oral tablets of Yocon<sup>®</sup> 1/12 gr. 5.4 mg in bottles of 100's NDC 53159-001-01 and 1000's NDC 53159-001-10.

### References:

1. A. Morales et al., New England Journal of Medicine: 1221, November 12, 1981.
2. Goodman, Gilman — The Pharmacological basis of Therapeutics 6th ed., p. 176-188. McMillan December Rev. 1/85.
3. Weekly Urological Clinical letter, 27:2, July 4, 1983.
4. A. Morales et al., The Journal of Urology 128: 45-47, 1982.

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# Letters

## **To The Editors, Journal MSMA:**

I am writing to comment on the review in the January issue of the journal under the title "*Date-line*". The news article review discusses the new recommendations for annual adolescent check-ups and how that may possibly reduce health care costs. I believe that most of us who care for adolescents would clearly agree with that guideline.

Two (2) years ago the association, at its annual meeting, passed a resolution indicating that athletic physicals should desirably be accomplished by the child's usual physician. The intent was to get the adolescent and pre-adolescent into the doctor's office during an age at which anticipatory guidance was severely needed on a number of subjects. The way that athletic exams are usually done, en mass, does not lend itself to such counseling and guidance. Also, adolescents who have had their "ball exam" are unlikely to come to their usual primary care physician for an annual health maintenance examination.

I believe that until we can rectify the way athletic physicals are done in most areas of the state, and probably the nation, adolescents who need counseling regarding health matters will not find themselves receiving it in their primary care physicians of-

fice, or at all.

I encourage members of the association to speak out in favor of privately accomplished sports physicals in conjunction with a annual health maintenance examination as the best way to accomplish these ends.

Sincerely,  
**R. Ray Lyle, MD**  
Starkville, MS

## **To The Editors, Journal MSMA:**

Our research group is in the process of accumulating data on the human health effects of nonionizing electromagnetic radiation. Specifically, we are interested in nonionizing electromagnetic frequencies in the range between electric power transmission frequencies, and microwave frequencies.

Although there has been a great deal of interest and research on this subject, the information available on the human health effects of this radiation does not permit us to conclude that there are serious health effects.

We believe there is an increase in awareness of both physicians and patients that nonionizing

electromagnetic radiation may have some human health effects, with the most prominent being links to neoplastic disease. Of specific interest to us is the potential for collecting cases or clusters of cases recognized by practicing physicians in the United States, which may be related to exposure to Nonionizing Electromagnetic Radiation.

We would be interested in hearing from any physicians or physician groups that may have experience with this problem.

Sincerely  
**Joseph R. Salvatore, MD**  
300 Tollgate Rd.  
Warwick, RI 02886  
(401) 732-4900

## **To The Journal MSMA:**

I am collecting information for publication on America's earliest physicians (particularly Jewish doctors), and early American medicine in your state, counties, cites, etc.

My period of interest extends from the earliest available material through the first quarter of the 19th century.

Do you have available information on these subjects (individual bios, medical education,

tion, early medical societies, medical staffs, etc.) and if not, could you refer me to any other sources that might be of help?

If there is a fee for copying/and or mailing, please enclose a bill at the time of mailing.

Very truly yours,

**Theodore Cohen, MD, FACP**  
186-30 Cambridge Road  
Jamaica Estates,  
New York 11432

**Dear Friends:**

We are overwhelmed with over 500 contributions to the Carl Gustav Evers Award Fund. Carl's entire medical career in Mississippi was one of zeal and passion for the University of Mississippi Medical Center and the Mississippi State Medical Association academia and organized medicine. He cherished the students, the teaching role, his MSMA associates and the medical "politics". The graduate re-

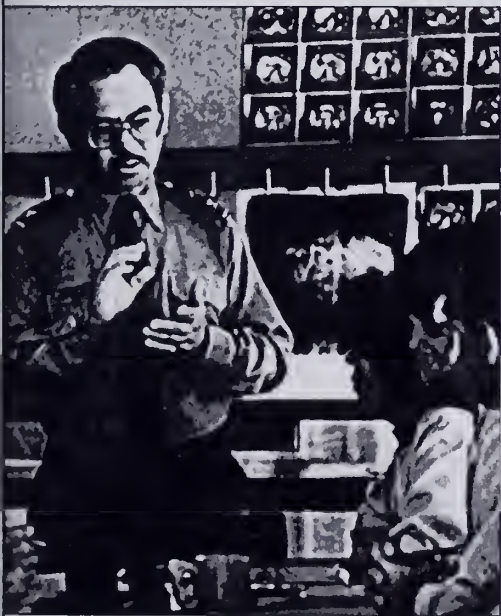
ceiving the Evers Award will be one emulating those characteristics of scholar and commitment to the profession.

For your contributions, letters, calls .... for your prayers, love and concern... for your attentiveness and vigil... we are grateful. Thank you for this most significant memorial and legacy.

God's blessing,

**Jan, Karen, Julie & Gus Evers**

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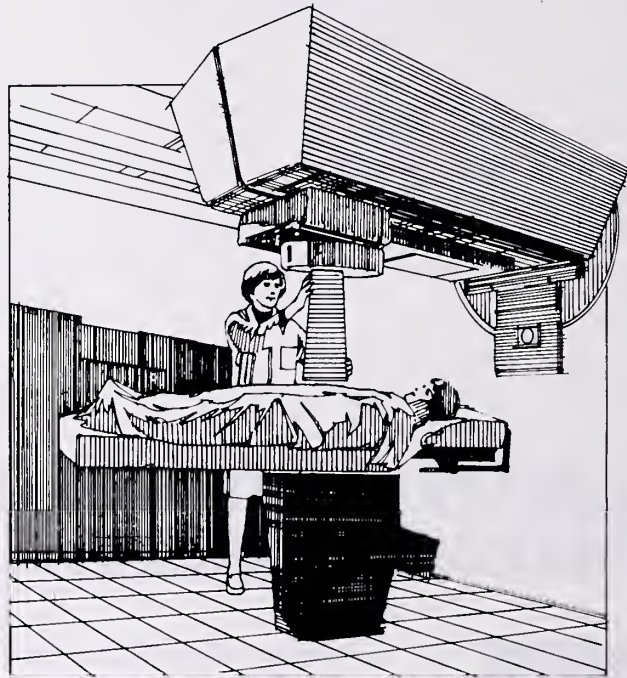
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---

# "Current Opinions"

of the Council on Ethical and  
Judicial Affairs of the American Medical Association

## Opinions on Professional Rights and Responsibilities

### Discipline and Medicine

**I**ncompetence, corruption or dishonest or unethical conduct on the part of members of the medical profession is reprehensible. In addition to posing a real or potential threat to patients, such conduct undermines the public's confidence in the profession. A physician should expose, without fear or favor, incompetent or corrupt, dishonest or unethical conduct on the part of members of the profession. Questions of such conduct should be considered, first, before proper medical tribunals in executive sessions or by special

or duly appointed committees on ethical relations, provided such a course is possible and provided, also, that the law is not hampered thereby. If doubt should arise as to the legality of the physician's conduct, the situation under investigation should be placed before officers of the law, and the physician-investigators should take the necessary steps to enlist the interest of the proper authority.

An ethical physician will observe the laws regulating the practice of medicine and will not assist others to evade such laws.

The Council cannot pass judgment in advance on a situation that may later come before it on appeal. The Council cannot be an attorney for a society or a member thereof and later judge in the same factual situation. The local medical society has the initial obligation of determining all the facts and whether or not disciplinary action is indicated. Questions asking for a review of a proposed course of action or an evaluation of an existing factual situation should be presented to the appropriate official of the physician's local society. □



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# Now is the critical time to help shape the President's plan for reform.

---

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---

The Clinton Administration has promised to develop a comprehensive health care reform plan during its first 100 days. President Clinton has recently appointed a White House Task Force on Health Care Reform, headed by Hillary Rodham Clinton, to develop a plan for submission to Congress. Now is the time for physicians to speak out to ensure that patients' needs remain the focus of system reform.

The American Medical Association (AMA) has initiated an unprecedented meeting between health care policy makers and physicians from across the

country. "A Time for New Partnership" will take place in Washington, DC, March 23-25. Your participation is critical.

Key individuals from the Administration and Congress will meet with us to discuss and debate our plan for reform, *Health Access America*, along with their proposed solutions. You will also have the chance to meet with elected Representatives from your region.

Speak out on behalf of patients. For more information, or to make reservations, call **800 262-3211**.

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# Medical Organization



*The MSMA Board of Trustees joined members of the Homochitto Valley Medical Society for their February Meeting. MSMA President, William C. Gates, MD, was guest speaker. The MSMA Board of Trustees held its February meeting in Natchez.*

*Attending the Homochitto Valley meeting were; above from left, MSMA President William C. Gates, Jr., MD; Mrs. Linda Gates; David G. Hall, MD, Homochitto Valley Medical Society Secretary; and Mal G. Morgan, MD, MSMA Chairman of the Board of Trustees, at the podium.*



*Fred Guidry, MD, an anesthesiologist practicing in Jackson, standing, spoke to UMC medical students recently about the specialty of anesthesiology. UMC Medical Alumni Association and MACM are sponsors of this monthly luncheon meeting at which students have the opportunity to hear practicing physicians talk about their specialty. The goal of the program is to give these students more insight into the day to day practice of various medical specialties.*

## Medical Organization



*MSMA President, William C. Gates, Jr., MD, above, was guest speaker at the February Central Medical Society meeting. Thomas C. Fenter, MD, at right, a Urologist and member of Central Medical Society enjoyed the opportunity of introducing Dr. Gates, a fellow urologist.*



*John J. Cook, MD, an emergency medicine physician in Jackson, is currently serving as Central Medical Society President.*



*Ninety physicians attended the February meeting of the Central Medical Society. In addition to Dr. Gates presentation, society members had the opportunity to hear Ms. Clare Hester, MSMA Director of Legislative Activities give an update on current legislative issues.*





# MSMA 125th Annual Session

## April 28 - May 2, 1993

### Royal d'Iberville Hotel • Biloxi, Mississippi

#### Program Overview

##### **Wednesday, April 28**

1:00 PM - Exhibitor Set-up - Technical and Scientific

##### **Thursday, April 29**

7:00 AM - Exhibits Open  
 8:00 AM - MSMA Registration Opens  
 9:00 AM - **MSMA HOUSE OF DELEGATES**  
 Noon - Committee on Publications Meeting  
 1:00 PM - Mississippi Foundation for Medical Care Membership Meeting  
 2:00 PM - The Young Physician's and Hospital Medical Staff Sections;  
                     Howard L. Lang, MD, Immediate Past Chair, AMA Hospital  
                     Medical Staff Section  
 3:30 PM - Young Physicians Section Business Meeting  
                     Hospital Medical Staff Section Business Meeting  
 4:00 PM - **MSMA REFERENCE COMMITTEE A**  
 6:00 PM - MSMA President's Reception - An Evening on The Isle of Capri

##### **Friday, April 30**

7:00 AM - Exhibits Open  
                     Fishing Rodeo  
                     University of Mississippi Medical Alumni Association Breakfast  
 7:30 AM - MS EENT Association Breakfast  
 8:00 AM - MSMA Registration Opens  
 8:00 AM - MSMA Past President's Breakfast  
 8:00 AM - **MEDICINE PLENARY SESSION**  
 9:00 AM - MSMA Auxiliary House of Delegates Meeting  
 11:30 AM - MS Association of Public Health Physicians  
             Noon - MS Academy of Family Physicians Luncheon  
                     MS Psychiatric Association Luncheon  
                     MS Society of Internal Medicine Luncheon  
                     MS Chapter, American Academy of Pediatrics Luncheon  
 1:00 PM - **MSMA REFERENCE COMMITTEE**  
                     **(CONSTITUTION and BY-LAWS)**  
 2:00 PM - **MSMA REFERENCE COMMITTEE B**  
 4:00 PM - MS Physicians Insurance Company Annual Stockholders Meeting  
 5:00 PM - Mississippi State University Medical Alumni Hospitality  
 5:30 PM - Medical Assurance Company of Mississippi Hospitality  
 6:00 PM - Tulane University Medical Alumni Association Meeting  
 6:30 PM - University of Mississippi Medical Alumni Association  
                     Sea Food Buffet



**Saturday, May 1**

- 7:00 AM - Fishing Rodeo
- 7:00 AM - ACS Officers and Board of Governors' Breakfast
- 7:30 AM - Cancer Liaison Physicians' Breakfast
- 8:00 AM - MSMA Registration Opens
- **SURGERY PLENARY SESSION**
- 8:30 AM - Fifty Year Club Breakfast
- 9:00 AM - MS Dermatological Society Meeting
- Noon - MS Chapter, American College of Surgeons Luncheon /Annual  
and Scientific Meetings
- MS Dermatological Society Luncheon
- MS Chapter, American College of Emergency Physicians  
Luncheon and Scientific Meeting
- MS Society of Anesthesiologists Luncheon
- MS Association of Pathologists Luncheon
- **Tennis Tournament - Gulfport Racquet Club**
- 1:00 PM - **Golf Tournament - Broadwater Sun Course**
- 6:30 PM - **MSMA and MSMA Auxiliary Membership Party -**  
Jazz and Hor d'oeuvres, Poolside

**Sunday, May 2**

- 7:30 AM - Continental Breakfast
- 8:00 AM - Protestant Church Service
- MSMA Registration Opens
- 9:00 AM - **MSMA HOUSE OF DELEGATES**
- Noon - Meeting Adjourns

## **"Health Care Reform... Challenges and Opportunities"**

### **Medicine and Surgery Plenary Sessions • April 30 - May 1, 1993 Preliminary Program**

**Medicine Plenary, April 30**

- 8:00 am - Scientific Presentations
- 10:00 am - "The Administration's Plans for Health Care Reform" - Mrs. Hillary Clinton has been  
invited to speak or a member of the Health Reform Task Force.
- "Managed Competition" - C. J. Bolster, Peat, Marwick and Mitchell
- "An HMO's View of Managed Competition" - Howard Waltman, SANUS  
Corporation Health System
- noon - Adjourn

**Surgery Plenary, May 1**

- 8:00 am - Scientific Presentation
- 9:00 am - "State Health Care Reform Strategies" - John E. Patchett, JD, Director, AMA  
Department State Legislation
- "Medicaid Its Present and Future" - Helen Wetherbee, Director, MS Division of  
Medicaid
- "Alternative Dispute Mechanisms" - Andy Warshaw, MD, Chief of General Surgery,  
Massachusetts General
- "Quality of Care/Outcomes Measurement" - Alton B. Cobb, MD, MFMC
- noon - Adjourn

# Personals

**Paul M. Allen** of Pascagoula has been invited by the Southern California Association of Health Care Risk Managers to conduct an educational session entitled, *Risk Management Issues in the Physician Office* at the group's annual educational meeting. He also participated as a visiting faculty member in a symposium entitled *The Fourth Decade of Oral Contraception* sponsored by the University of Minnesota, Office of Continuing Medical Education, and held in Washington, DC in February.

**Michael Stuart Ballentine** of Clarksdale has become a Certified Diplomate of The American Board of Obstetrics and Gynecology.

**O. J. Briseno** of Union has associated with the Family Medical Clinic of Decatur.

**C. Ron Cannon** of Jackson has been recommended for election to Active Fellowship in the Triological Society. His thesis was accepted by the society and received Honorable Mention for its excellence. He will receive an Award Certificate at the annual meeting of the Triological Society in Los Angeles, in April.

**C. Ralph Daniel, III**, of Jackson recently made presentations in San Francisco on *Pediatric Nail Disorders* and in Dallas on *Laboratory Monitoring During Systemic Antifungal Therapy*.

**Jim Gordan** of Tupelo has received the following invitations: Speaker at the International BPH, Prostate, and Genital Urinary Cancer, in February; Reviewer for *Urology*; Faculty member of AUA Surgical Learning Center, in April; and writer for *Urology Times* on *TULIP*.

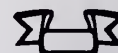
**Michael D. Horowitz**, a cardiovascular surgeon, has joined the staff of Singing River Hospital, Pascagoula.

**Ken Lippincott** of Tupelo completed the requirements for board certification in Psychiatry, "Diplomate, American Board of Psychiatry and Neurology."

**Andrew Martinolich** of Biloxi has been elected chief of staff for Hancock Medical Center in Bay St. Louis.

**Daniel J. Peasley** and **Stephen P. Johnson** of the Gastroenterology Clinic in Laurel are forming a support group for persons suf-

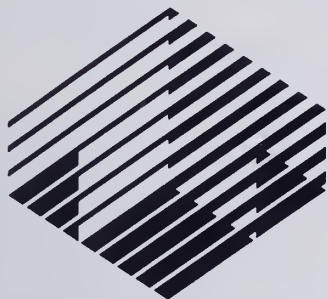
## Physicians' Recognition Award



Two MSMA members were named recipients of the AMA Physicians' Recognition Award in January 1993. This award is presented by the American Medical Association to Physicians who have voluntarily completed a specified number of continuing medical education hours. These individuals are presented below by medical society.

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Medical Society  
**Jimmy E. Isbell, MD**

Northeast Mississippi  
Medical Society  
**Elbert A. White, MD**



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Olive Branch/Pearl/Pelahatchie/Petal/Ridland/Ridgeland/Southaven  
Tylertown/Wesson

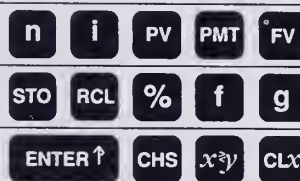
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**Personals/continued**

fering from Crohn's Disease and  
Ulcerative Colitis.

**Thomas N. Skelton**, associate  
professor of medicine at UMC  
will serve as American College  
of Cardiology Governor for Mis-  
sissippi from March 1993  
through March 1996. Dr. Skelton  
has served as governor-elect  
since March 1992.

**J. Tate Thigpen** of Jackson has  
been elected president of the Op-  
timist International Foundation,  
the charitable foundation of Op-  
timist International, for 1992-93.

**Matthew B. Wesson** an oph-  
thalmologist in Tupelo was one  
of six surgeons who presented  
case histories in prestigious  
Royal Hawaiian Eye Meeting.  
*Ophthalmology In Transition*  
was his topic in which he dis-  
cussed changes in the profession  
as related to the region in which  
his practice is located.

**William D. Young** of Waynesboro  
announces the opening of his  
practice in General Surgery,  
Wayne General Hospital, Medi-  
cal Arts Building, 940 Mathew  
Drive, Suite 7. □

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# Meetings

## NATIONAL AND REGIONAL

**American Medical Association**, Annual Meeting, June 13 - 17, 1993  
Chicago; Interim, December 5 - 8, New Orleans, LA James S. Todd,  
MD, Executive Vice President, 515 N. State St., Chicago, IL 60610

## STATE AND LOCAL

**Mississippi State Medical Association**, 125th Annual Session, April  
28-May 2, 1993, Biloxi, Charles L. Mathews, Executive Director,  
735 Riverside Drive, PO Box 5229, Jackson 39296-5229.

**Mississippi Academy of Family Physicians**, Annual Meeting, July 28-  
31, 1993, Destin, FL. Leontine Stevens, Executive Secretary, PO Box  
1215 Ridgeland 39158.

**Amite-Wilkinson Counties Medical Society**, 3rd Monday, March, June,  
September, December, James S. Poole, MD, Secy., The Gloster Clinic,  
PO Box D, Gloster 39638. Counties: Amite, Wilkinson.

**Central Medical Society**, 1st Tuesday, February, April, October, De-  
cember, 6:30 p.m., Primos Northgate Restaurant, Jackson. Patsy  
Douglas, Executive Secy., 735 Riverside Dr., Jackson 39202. Coun-  
ties: Hinds, Leake, Madison, Rankin, Scott, Simpson.

**Clarksdale and Six Counties Medical Society**, 3rd Wednesday, April,  
and 1st Wednesday, November, 2:00 p.m., Clarksdale, Glen L.  
Wegener, MD, Secy., PO Box 430, Clarksdale, MS 38614-0430.  
Counties: Coahoma, Quitman, Tallahatchie, Tunica.

**Coast Counties Medical Society**, January, March, June, and November.  
James E. Clarkson, MD, Secy., Mail: Ms. Leslie Johnson, PO Box  
128, Biloxi 39533. Counties: Hancock, Harrison.

**Delta Medical Society**, 2nd Wednesday, April and October. Walter H.  
Rose, MD, Secy., 122 E. Baker St., Indianola 38751. Counties: Boli-  
var, Humphreys, Leflore, Sunflower, Washington, Yazoo.

**East Mississippi Medical Society**, 1st Tuesday, February, April, June,  
October, December. Charles L. Wilkinson, MD, Secy., Mail: Ms.  
Jenkins, PO Box 4053, West Station, Meridian 39305. Counties:  
Clarke, Kemper, Lauderdale, Neshoba, Newton, Winston.

**Homochitto Valley Medical Society**. Meetings scheduled quarterly,  
David G. Hall, MD, Secy., 150 Jeff Davis Blvd, Suite 130, Natchez  
39120. Counties: Adams, Jefferson.

**North Central District Medical Society**, 3rd Wednesday, March, June,  
September, January, Gary Holdiness, MD, 332 Hwy 12 W, Kosciusko  
39090. Counties: Attala, Carroll, Choctaw, Granada, Holmes, Mon-  
tgomery, Webster.

**Northeast Mississippi Medical Society**, 1st Thursday, March, June,  
September, December. Richard L. Heyer, Jr., MD, Secy., Mail: Ms.  
Shirley Irwin, PO Box 3294, Tupelo 38803-3294. Counties: Alcorn,  
Calhoun, Chickasaw, Itawamba, Lee, Monroe, Pontotoc, Prentiss,  
Tishomingo, Union.

**North Mississippi Medical Society**, 1st Thursday, April, September, and  
3rd Thursday, January. Catherine E. Gleason, MD, Secy., 1306 Belk  
Blvd., Oxford 38655. Counties: Benton, Lafayette, Marshall, Panola,  
Tate, Tippah, Yalobusha.

**Prairie Medical Society**, 2nd Tuesday, March, June, September, De-  
cember, Joseph S. Boggess, MD, Secy., 515 Willowbrook Rd., Co-  
lumbus, MS 39701. Counties: Clay, Oktibbeha, Noxubee, Lowndes.

**Singing River Medical Society**, Quarterly, December, March, June and  
September. Hal Moore, MD, Secy., Mail: Ms. Beverly Small, 3003  
Shortcut Rd, Pascagoula 39567. County: Jackson.

**South Central Mississippi Medical Society**, 2nd Tuesday, March, June,  
September, December. Julian T. Janes, Jr., MD, Secy., PO Box 1910,  
McComb 39648. Counties: Copiah, Franklin, Lawrence, Lincoln,  
Pike, Walthall.

**South Mississippi Medical Society**, 2nd Thursday, March, June, Sep-  
tember, December. William A. Whitehead, MD, 415 South 28th  
Ave., Hattiesburg 39401-7246. Counties: Covington, Forrest, George,  
Greene, Jasper, Jefferson Davis, Jones, Lamar, Marion, Perry, Smith,  
Wayne.

**West Mississippi Medical Society**, 2nd Tuesday, January, May, Sep-  
tember, November, 6:30 p.m. Maxwell's Restaurant, Vicksburg.  
Chester Masterson, MD, Secy., 1901 Mission 66, Vicksburg 39180.  
Counties: Issaquena, Sharkey, Warren.

## Mississippi Institutions and Organizations Accredited for Continuing Medical Education

The following Mississippi institutions and medical organizations  
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the individual institution or organization.

Council on Scientific Assembly Mississippi State Medical Association 735 Riverside Drive Jackson, MS 39202-1166	Golden Triangle Regional Medical Center 2520 Fifth St., North Columbus, MS 39701
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North Mississippi Medical Center 830 Gloster Street Tupelo, MS 38801	Northwest Mississippi Regional Medical Center Hospital Dr. Clarksdale, MS 38614
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Forrest General Hospital Mamie Street and Highway 49 South Hattiesburg, MS 39401	Singing River Hospital 2809 Denny Ave. Pascagoula, MS 39567
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Mississippi Baptist Medical Center 1225 N. State Street Jackson, MS 39202	Greenwood Leflore Hospital 1401 River Rd. Greenwood, MS 38930
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Gulf Coast Community Hospital 180 DeBuys Rd. Biloxi, MS 39531	Memorial Hospital at Gulfport 4500 13th St. Gulfport, MS 39501
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Jefferson Davis Memorial Hospital Sergeant Prentiss Drive Natchez, MS 39120	Baptist Memorial Hospital of North Mississippi Highway 7, South Oxford, MS 38655
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Charter Hospital of Jackson Lakeland Drive Jackson, MS 39208	Delta Regional Medical Center 1400 E. Union Greenville, MS 39704
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Biloxi Regional Medical Center 150 Reynoir St. Biloxi, MS 39533	Methodist Hospital 5001 W. Hardy St. Hattiesburg, MS 39401
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Jeff Anderson Regional Medical Center 2124 14th St. Meridian, MS 39301	MS State Department of Health PO Box 1700 Jackson, MS 39215-1700
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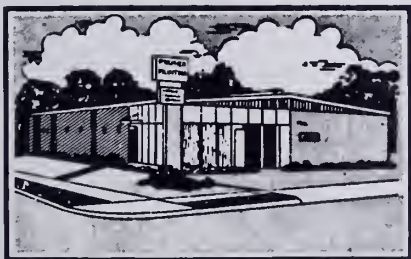
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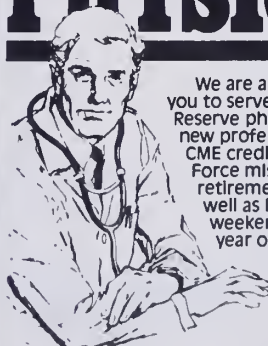
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## Index to Advertisers

Avanti .....	8
Bristol-Myers Squibb Company - Pravachol .....	third and fourth cover
CancerPay Plus .....	92
CompHealth .....	85
Disability Determination .....	104
Eli Lilly & Co. - Humulin .....	76
Employer Plus, Inc. ....	4
Medical Assurance Co. of MS .....	5
Medley & Company .....	101
MS Emergency Association .....	104
MS Methodist Rehabilitation Center .....	second cover
MS Physicians Insurance Company .....	89
MSMA Benefit Plan & Trust .....	82
Palisades Pharmaceuticals, Inc. - Yocon .....	88
Premier Printing .....	105
PRI-MED, Inc. ....	105
The Doctors' Company .....	94
Trustmark .....	101
US Air Force Reserve .....	105
US Army Active .....	75
US Army Reserve .....	91



# CONTRAINDICATIONS

Sensitivity to any component of this medication.

liver disease or unexplained, persistent elevations in liver function tests (see WARNINGS).

agnancy and lactation. Atherosclerosis is a chronic process and discontinuation of lipid-lowering drugs during pregnancy should have little impact on the outcome of long-term therapy of primary hypercholesterolemia. Other and other products of cholesterol biosynthesis are essential components for fetal development (including synthesis of steroids and cell membranes). Since HMG-CoA reductase inhibitors decrease cholesterol synthesis and possibly the synthesis of other biologically active substances derived from cholesterol, they may be fetal harm when administered to pregnant women. Therefore, HMG-CoA reductase inhibitors are contraindicated during pregnancy and in nursing mothers. **Pravastatin should be administered to women of child-bearing age only when such patients are highly unlikely to conceive and have been informed of the potential hazards.** If the patient becomes pregnant while taking this class of drug, therapy should be discontinued and the patient apprised of the potential hazard to the fetus.

# WARNINGS

**Enzymes:** HMG-CoA reductase inhibitors, like some other lipid-lowering therapies, have been associated with biochemical abnormalities of liver function. Increases of serum transaminase (ALT, AST) values to more than three times the upper limit of normal occurring on 2 or more (not necessarily sequential) occasions have been reported in 1.3% of patients treated with pravastatin in the U.S. over an average period of 18 months. These abnormalities were not associated with cholestasis and did not appear to be related to treatment duration. In patients in whom these abnormalities were believed to be related to pravastatin and who were discontinued from therapy, the transaminase levels usually fell slowly to pretreatment levels. These biochemical findings are only asymptomatic, although worldwide experience indicates that anorexia, weakness, and/or abdominal pain can also be present in rare patients.

With other lipid-lowering agents, liver function tests should be performed during therapy with pravastatin. Serum aminotransferases, including ALT (SGPT), should be monitored before treatment begins, every six weeks for the first three months, every eight weeks during the remainder of the first year, and periodically thereafter (e.g., about six-month intervals). Special attention should be given to patients who develop increased transaminase levels. Liver function tests should be repeated to confirm an elevation and subsequently monitored at more frequent intervals. If increases in AST and ALT equal or exceed three times the upper limit of normal and persist, therapy should be discontinued. Persistence of significant aminotransferase elevations following discontinuation of therapy may warrant consideration of liver biopsy.

Active liver disease or unexplained transaminase elevations are contraindications to the use of pravastatin (see CONTRAINDICATIONS). Caution should be exercised when pravastatin is administered to patients with a history of liver disease or heavy alcohol ingestion (see CLINICAL PHARMACOLOGY: Pharmacokinetics/Metabolism). Such patients should be closely monitored, started at the lower end of the recommended dosing range, and treated to the desired therapeutic effect.

**Skeletal Muscle:** Rhabdomyolysis with renal dysfunction secondary to myoglobinuria has been reported with pravastatin and other drugs in this class. Uncomplicated myalgia has also been reported in pravastatin-treated patients (see ADVERSE REACTIONS). Myopathy, defined as muscle aches or muscle weakness in conjunction with increases in creatine phosphokinase (CPK) values to greater than 10 times the upper limit of normal was reported to be possibly due to pravastatin in only one patient in clinical trials (<0.1%). Myopathy should be considered in any patient with diffuse myalgias, muscle tenderness or weakness, and/or marked weakness. Patients should be advised to report promptly unexplained muscle pain, tenderness or weakness, particularly if accompanied by malaise or fever. **Pravastatin therapy should be discontinued if markedly elevated CPK levels occur or myopathy is diagnosed or suspected. Pravastatin therapy should be temporarily withheld in any patient experiencing an acute or serious condition predisposing to the development of renal failure secondary to rhabdomyolysis, e.g., sepsis; hypotension; major surgery; trauma; severe metabolic, endocrine, or electrolyte disorders; or uncontrolled epilepsy.**

The risk of myopathy during treatment with lovastatin is increased if therapy with either cyclosporine, gemfibrozil, erythromycin, or niacin is administered concurrently. There is no experience with the use of pravastatin together with cyclosporine. Myopathy has not been observed in clinical trials involving small numbers of patients who were treated with pravastatin together with niacin. One trial of limited size involving combined therapy with pravastatin and gemfibrozil showed a trend toward more frequent CPK elevations and patient withdrawals due to musculoskeletal symptoms in the group receiving combined treatment as compared with the groups receiving aceto, gemfibrozil, or pravastatin monotherapy. Myopathy was not reported in this trial (see PRECAUTIONS: Drug Interactions). One patient developed myopathy when clofibrate was added to a previously well tolerated regimen of pravastatin; the myopathy resolved when clofibrate therapy was stopped and pravastatin treatment continued. **The use of fibrates alone may occasionally be associated with myopathy. The combined use of pravastatin and fibrates should generally be avoided.**

# PRECAUTIONS

**General:** Pravastatin may elevate creatine phosphokinase and transaminase levels (see ADVERSE REACTIONS). It should be considered in the differential diagnosis of chest pain in a patient on therapy with pravastatin.

**Homozygous Familial Hypercholesterolemia.** Pravastatin has not been evaluated in patients with rare homozygous familial hypercholesterolemia. In this group of patients, it has been reported that HMG-CoA reductase inhibitors are less effective because the patients lack functional LDL receptors.

**Renal Insufficiency.** A single 20 mg oral dose of pravastatin was administered to 24 patients with varying degrees of renal impairment (as determined by creatinine clearance). No effect was observed on the pharmacokinetics of pravastatin or its 3 $\alpha$ -hydroxy isomeric metabolite (SQ 31,906). A small increase was seen in mean AUC values and half-life ( $t_{1/2}$ ) for the inactive enzymatic ring hydroxylation metabolite (SQ 31,945). Given this small sample size, the dosage administered, and the degree of individual variability, patients with renal impairment who are receiving pravastatin should be closely monitored.

**Information for Patients:** Patients should be advised to report promptly unexplained muscle pain, tenderness or weakness, particularly if accompanied by malaise or fever.

**Drug Interactions:** Immunosuppressive Drugs, Gemfibrozil, Niacin (Nicotinic Acid), Erythromycin: See WARNINGS: Skeletal Muscle.

**Antipyrine:** Clearance by the cytochrome P450 system was unaltered by concomitant administration of pravastatin. Since pravastatin does not appear to induce hepatic drug-metabolizing enzymes, it is not expected that any significant interaction of pravastatin with other drugs (e.g., phenytoin, quinidine) metabolized by the cytochrome P450 system will occur.

**Cholestyramine/Colestipol:** Concomitant administration resulted in an approximately 40 to 50% decrease in the mean AUC of pravastatin. However, when pravastatin was administered 1 hour before or 4 hours after cholestyramine or 1 hour before colestipol and a standard meal, there was no clinically significant decrease in bioavailability or therapeutic effect. (See DOSAGE AND ADMINISTRATION: Concomitant Therapy.)

**Warfarin:** In a study involving 18 healthy male subjects given pravastatin and warfarin concomitantly for 6 days, bioavailability parameters at steady state for pravastatin (parent compound) were not altered. Pravastatin did not alter the plasma protein-binding of warfarin. Concomitant dosing did increase the AUC and C<sub>max</sub> of warfarin but did not produce any changes in its anticoagulant action (i.e., no increase was seen in mean prothrombin time after 6 days of concomitant therapy). However, bleeding and extreme prolongation of prothrombin time has been reported with another drug in this class. Patients receiving warfarin-type anticoagulants should have their prothrombin times closely monitored when pravastatin is initiated or the dosage of pravastatin is changed.

**Cimetidine:** The AUC<sub>0-12h</sub> for pravastatin when given with cimetidine was not significantly different from the AUC for pravastatin when given alone. A significant difference was observed between the AUC's for pravastatin when given with cimetidine compared to when administered with antacid.

**Digoxin:** In a crossover trial involving 18 healthy male subjects given pravastatin and digoxin concurrently for 9 days, the bioavailability parameters of digoxin were not affected. The AUC of pravastatin tended to increase, but the overall bioavailability of pravastatin plus its metabolites SQ 31,906 and SQ 31,945 was not altered.

**Gemfibrozil:** In a crossover study in 20 healthy male volunteers given concomitant single doses of pravastatin and gemfibrozil, there was a significant decrease in urinary excretion and protein binding of pravastatin. In addition, there was a significant increase in AUC, C<sub>max</sub>, and T<sub>max</sub> for the pravastatin metabolite SQ 31,906. Combination therapy with pravastatin and gemfibrozil is generally not recommended.

In interaction studies with aspirin, antacids (1 hour prior to PRAVACHOL), cimetidine, nicotinic acid, or probucol, no statistically significant differences in bioavailability were seen when PRAVACHOL (pravastatin sodium) was administered.

**Other Drugs:** During clinical trials, no noticeable drug interactions were reported when PRAVACHOL was added to: diuretics, antihypertensives, digitalis, converting-enzyme inhibitors, calcium channel blockers, beta-blockers, or nitroglycerin.

**Endocrine Function:** HMG-CoA reductase inhibitors interfere with cholesterol synthesis and lower circulating cholesterol levels and, as such, might theoretically blunt adrenal or gonadal steroid hormone production. Results of clinical trials with pravastatin in males and post-menopausal females were inconsistent with regard to possible effects of the drug on basal steroid hormone levels. In a study of 21 males, the mean testosterone response to human chorionic gonadotropin was significantly reduced ( $p<0.004$ ) after 16 weeks of treatment with 40 mg of pravastatin. However, the percentage of patients showing a  $\geq 50\%$  rise in plasma testosterone after human chorionic gonadotropin stimulation did not change significantly after therapy in these patients. The effects of HMG-CoA reductase inhibitors on spermatogenesis and fertility have not been studied in adequate numbers of patients. The effects, if any, of pravastatin on the pituitary-gonadal axis in pre-menopausal females are unknown. Patients treated with pravastatin who display clinical evidence of endocrine dysfunction should be evaluated appropriately. Caution should also be exercised if an HMG-CoA reductase inhibitor or other agent used to lower cholesterol levels is administered to patients also receiving other drugs (e.g., ketoconazole, spiro lactone, cimetidine) that may diminish the levels or activity of steroid hormones.

**CNS Toxicity:** CNS vascular lesions, characterized by perivascular hemorrhage and edema and mononuclear cell infiltration of perivascular spaces, were seen in dogs treated with pravastatin at a dose of 25 mg/kg/day, a dose that produced a plasma drug level about 50 times higher than the mean drug level in humans taking 40 mg/day. Similar CNS vascular lesions have been observed with several other drugs in this class.

A chemically similar drug in this class was produced optic nerve degeneration (Wallerian degeneration of retinogeniculate fibers) in clinically normal dogs in a dose-dependent fashion starting at 60 mg/kg/day, a dose that produced mean plasma drug levels about 30 times higher than the mean drug level in humans taking the highest recommended dose (as measured by total enzyme inhibitory activity). This same drug also produced vestibulocochlear Wallerian-like degeneration and retinal ganglion cell chromatolysis in dogs treated for 14 weeks at 180 mg/kg/day, a dose which resulted in a mean plasma drug level similar to that seen with the 60 mg/kg dose.

**Carcinogenesis, Mutagenesis, Impairment of Fertility:** In a 2-year study in rats fed pravastatin at doses of 10, 30, or 100 mg/kg body weight, there was an increased incidence of hepatocellular carcinomas in males at the highest dose ( $p<0.01$ ). Although rats were given up to 125 times the human dose (HD) on a mg/kg body weight basis, their serum drug levels were only 6 to 10 times higher than those measured in humans given 40 mg pravastatin as measured by AUC.

The oral administration of 10, 30, or 100 mg/kg (producing plasma drug levels approximately 0.5 to 5.0 times human drug levels at 40 mg) of pravastatin to mice for 22 months resulted in a statistically significant increase in the incidence of malignant lymphomas in treated females when all treatment groups were pooled and compared to controls ( $p<0.05$ ). The incidence was not dose-related and male mice were not affected.

A chemically similar drug in this class was administered to mice for 72 weeks at 25, 100, and 400 mg/kg body weight, which resulted in mean serum drug levels approximately 3, 15, and 33 times higher than the mean human serum drug concentration (as total inhibitory activity) after a 40 mg oral dose. Liver carcinomas were significantly increased in high-dose females and mid- and high-dose males, with a maximum incidence of 90 percent in males. The incidence of adenomas of the liver was significantly increased in mid- and high-dose females. Drug treatment also significantly increased the incidence of lung adenomas in mid- and high-dose males and females. Adenomas of the eye Harderian gland (a gland of the eye of rodents) were significantly higher in high-dose mice than in controls.

No evidence of mutagenicity was observed *in vitro*, with or without rat-liver metabolic activation, in the following studies: microbial mutagen tests, using mutant strains of *Salmonella typhimurium* or *Escherichia coli*; a forward mutation assay in L5178Y TK + / - mouse lymphoma cells; a chromosomal aberration test in hamster cells; and a gene conversion assay using *Saccharomyces cerevisiae*. In addition, there was no evidence of mutagenicity in either a dominant lethal test in mice or a micronucleus test in mice.

In a study in rats, with daily doses up to 500 mg/kg, pravastatin did not produce any adverse effects on fertility or general reproductive performance. However, in a study with another HMG-CoA reductase inhibitor, there was decreased fertility in male rats treated for 34 weeks at 25 mg/kg body weight, although this effect was not observed in a subsequent fertility study when this same dose was administered for 11 weeks (the entire cycle of spermatogenesis, including epididymal maturation). In rats treated with this same reductase inhibitor at 180 mg/kg/day, seminiferous tubule degeneration (necrosis and loss of spermatogenic epithelium) was observed. Although not seen with pravastatin, two similar drugs in this class caused drug-related testicular atrophy, decreased spermatogenesis, spermatocytic degeneration, and giant cell formation in dogs. The clinical significance of these findings is unclear.

**Pregnancy: Pregnancy Category X:** See CONTRAINDICATIONS.

Safety in pregnant women has not been established. Pravastatin was not teratogenic in rats at doses up to 1000 mg/kg/day or in rabbits at doses of up to 50 mg/kg/day. These doses resulted in 20x (rabbit) or 240x (rat) the human exposure based on surface area (mg/meter<sup>2</sup>). However, in studies with another HMG-CoA reductase inhibitor, skeletal malformations were observed in rats and mice. PRAVACHOL (pravastatin sodium) should be administered to women of child-bearing potential only when such patients are highly unlikely to conceive and have been informed of the potential hazards. If the woman becomes pregnant while taking PRAVACHOL (pravastatin sodium), it should be discontinued and the patient advised again as to the potential hazards to the fetus.

**Nursing Mothers:** A small amount of pravastatin is excreted in human breast milk. Because of the potential for serious adverse reactions in nursing infants, women taking PRAVACHOL should not nurse (see CONTRAINDICATIONS).

**Pediatric Use:** Safety and effectiveness in individuals less than 18 years old have not been established. Hence, treatment in patients less than 18 years old is not recommended at this time. (See also PRECAUTIONS: General.)

# ADVERSE REACTIONS

Pravastatin is generally well tolerated, adverse reactions have usually been mild and transient. In 4-month long placebo-controlled trials, 1.7% of pravastatin-treated patients and 1.2% of placebo-treated patients were discontinued from treatment because of adverse experiences attributed to study drug therapy, this difference was not statistically significant. In long-term studies, the most common reasons for discontinuation were asymptomatic serum transaminase increases and mild, non-specific gastrointestinal complaints. During clinical trials the overall incidence of adverse events in the elderly was not different from the incidence observed in younger patients.

**Adverse Clinical Events:** All adverse clinical events (regardless of attribution) reported in more than 2% of pravastatin-treated patients in the placebo-controlled trials are identified in the table below; also shown are the percentages of patients in whom these medical events were believed to be related or possibly related to the drug.

Body System/Event	All Events %		Events Attributed to Study Drug %	
	Pravastatin (N=900)	Placebo (N=411)	Pravastatin (N=900)	Placebo (N=411)
Cardiovascular				
Cardiac Chest Pain	4.0	3.4	0.1	0.0
Dermatologic				
Rash	4.0*	1.1	1.3	0.9
Gastrointestinal				
Nausea/Vomiting	7.3	7.1	2.9	3.4
Diarrhea	6.2	5.6	2.0	1.9
Abdominal Pain	5.4	6.9	2.0	3.9
Constipation	2.7	2.4	2.4	5.1
Flatulence	3.8	3.8	2.7	3.4
Heartburn	2.9	1.9	2.0	0.7
General				
Fatigue	3.8	3.4	1.9	1.0
Chest Pain	3.7	3.7	0.3	0.2
Influenza	2.4*	2.4	0.0	0.0
Musculoskeletal				
Localized Pain	10.0	9.0	1.4	1.5
Myalgia	2.7	1.0	0.6	0.0
Nervous System				
Headache	6.9	6.9	1.7*	0.2
Dizziness	3.3	3.3	1.0	0.5
Renal/Genitourinary				
Urinary Abnormality	2.4	2.9	0.7	1.2
Respiratory				
Common Cold	7.0	6.3	0.0	0.0
Rhinitis	4.0	4.1	0.1	0.0
Cough	2.6	1.7	0.1	0.0

\*Statistically significantly different from placebo.

The following effects have been reported with drugs in this class:

**Skeletal:** myopathy, rhabdomyolysis.

**Neurological:** dysfunction of certain cranial nerves (including alteration of taste, impairment of extra-ocular movement, facial paresis), tremor, vertigo, memory loss, paresthesia, peripheral neuropathy, peripheral nerve palsy.

**Hypersensitivity Reactions:** An apparent hypersensitivity syndrome has been reported rarely which has included one or more of the following features: anaphylaxis, angioedema, lupus erythematosus-like syndrome, polymyalgia rheumatica, vasculitis, purpura, thrombocytopenia, leukopenia, hemolytic anemia, positive ANA, ESR increase, arthritis, arthralgia, urticaria, asthenia, photosensitivity, fever, chills, flushing, malaise, dyspnea, toxic epidermal necrolysis, erythema multiforme, including Stevens-Johnson syndrome.

**Gastrointestinal:** pancreatitis, hepatitis, including chronic active hepatitis, cholestatic jaundice, fatty change in liver, and, rarely, cirrhosis, fulminant hepatic necrosis, and hepatoma, anorexia, vomiting.

**Reproductive:** gynecomastia, loss of libido, erectile dysfunction.

**Eye:** progression of cataracts (lens opacities), ophthalmoplegia.

**Laboratory Test Abnormalities:** Increases in serum transaminase (ALT, AST) values and CPK have been observed (see WARNINGS).

Transient, asymptomatic eosinophilia has been reported. Eosinophil counts usually returned to normal despite continued therapy. Anemia, thrombocytopenia, and leukopenia have been reported with other HMG-CoA reductase inhibitors.

**Concomitant Therapy:** Pravastatin has been administered concurrently with cholestyramine, colestipol, nicotinic acid, probucol and gemfibrozil. Preliminary data suggest that the addition of either probucol or gemfibrozil to therapy with lovastatin or pravastatin is **not associated** with greater reduction in LDL-cholesterol than that achieved with lovastatin or pravastatin alone. No adverse reactions unique to the combination or in addition to those previously reported for each drug alone have been reported. Myopathy and rhabdomyolysis (with or without acute renal failure) have been reported when another HMG-CoA reductase inhibitor was used in combination with immunosuppressive drugs, gemfibrozil, erythromycin, or lipid-lowering doses of nicotinic acid. Concomitant therapy with HMG-CoA reductase inhibitors and these agents is generally not recommended. (See WARNINGS: Skeletal Muscle and PRECAUTIONS: Drug Interactions.)

# OVERDOSAGE

There have been no reports of overdoses with pravastatin.

Should an accidental overdose occur, treat symptomatically and institute supportive measures as required. (J4-422A)

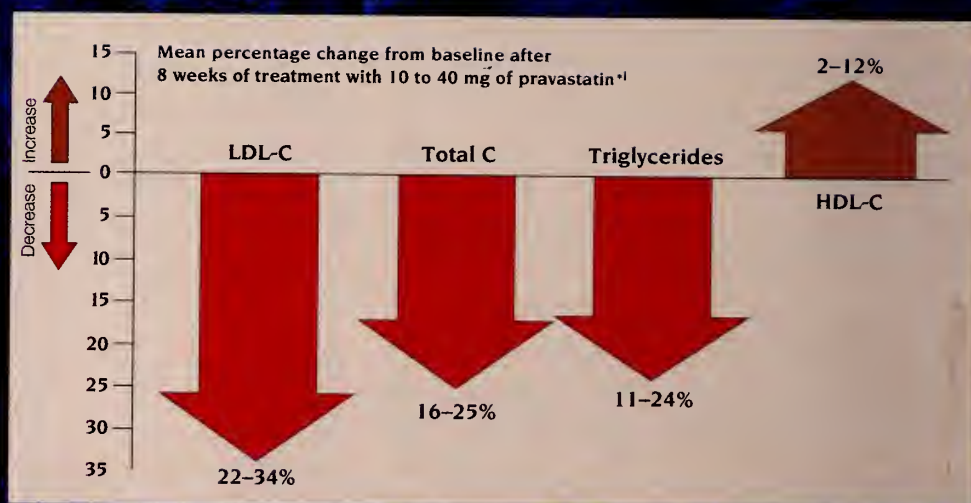






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<sup>\*1</sup>Each arrow represents a range of means derived from a single placebo-controlled study that included 55 patients treated with pravastatin.

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Active liver disease or unexplained transaminase elevations, pregnancy and lactation are contraindications to the use of pravastatin.

**Reference:** 1. Jones PH, et al. Once-daily pravastatin in patients with primary hypercholesterolemia: a dose-response study. *Clin Cardiol.* 1991;14:146-151.

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## SCIENTIFIC ARTICLES

- Aplastic Crisis Due To Human Parvovirus (B19)  
As An Initial Presentation of Hereditary  
Spherocytosis** 107  
*Gail C. Megason, MD; J. Clinton Smith, MD, MPH  
and Rath V. Iyer, MD*
- Clinicopathologic Conference I** 111  
*Joe C. Files, MD, Editor, et al.*

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## SPECIAL ARTICLE

- 125th Annual Session** 115

## EDITORIALS

- Reform Revisited** 120  
*William C. Gates, Jr., MD*
- Waiting For The Windfall** 121  
*Myron W. Lockey, MD, Editor*

## DEPARTMENTS

- Current Opinions** 123
- Medical Organization** 126
- New Members** 133
- Deaths** 134
- Personals** 135
- Placement Service** 138
- Classified** 140

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# Dateline

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## Recommendations for HIV Testing Services for Inpatients and Outpatients in Acute-Care Hospital Settings.

CDC has published revised recommendations for human immunodeficiency virus (HIV) counseling and testing of patients in acute-care hospital settings.<sup>1\*</sup> These recommendations update previous CDC guidelines published in 1987<sup>2</sup> and strengthen the recommendation for hospitals to assess the rate of HIV infection among their patient populations and to develop HIV-testing programs that assist infected patients in obtaining HIV-related treatment and prevention services. The revision was prompted by information regarding both the rates of previously unrecognized HIV infection among persons admitted to some acute-care hospitals and the potential medical and public health benefits of recognizing HIV infection in persons who have not developed acquired immunodeficiency syndrome (AIDS).

CDC recommends that hospitals and associated clinics encourage health-care providers to routinely ask patients in nonemergency settings about their risks for HIV infection. Patients at risk should be offered HIV counseling and testing services with informed consent obtained in accordance with local laws. In addition, hospitals with an HIV-seroprevalence rate of at least 1% or an AIDS diagnosis rate  $\geq 1.0$  per 1000 discharges<sup>3</sup> should strongly consider adopting a policy of offering such services routinely to patients aged 15-54 years. These services should be structured to facilitate confidential, voluntary patient participation and should include pretest information about the testing procedures, appropriate posttest counseling for infected patients and those at increased risk, and referral of HIV-infected persons for medical evaluation. Persons who decline HIV testing or who consent to testing and are found to be infected must not be denied needed health care or provided suboptimal care.

The recommendations emphasize that HIV counseling and testing programs should not be used as a substitute for universal precautions or other infection-control techniques and underscore the importance of effective and ongoing collaboration between acute-care providers and health departments to improve HIV-related prevention and treatment services.

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(continued)



**Extract:** Morbidity and Mortality Weekly Report (MMWE) March 5, 1993/Vol. 42/No. 8, pp. 157-158. Single Copies of the full report (January 15, 1993/Vol.42/No.RR-2) may be obtained by calling the CDC National AIDS Clearinghouse toll free at (800) 458-5231.

\*\*\*

## **MFMC Sets Review Physician Workshop**

The Mississippi Foundation for Medical Care is presenting a **Fourth Scope of Work Review Physician workshop** Thursday, April 29, at 3:45 p.m. in Biloxi.

The workshop will be held during the MSMA Annual Session at the Royal d'Iberville Hotel. Participation is limited and pre-registration is necessary. Please call the MFMC Communications Department at 354-0304 to register for the workshop.

CME credits will be available.

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## **State, Clinics Reach Abortion Accord**

Jackson, MS — Two Mississippi abortion clinics that perform abortions past 16 weeks of pregnancy have agreed to keep a registered nurse on call at all hours in an agreement with state health authorities.

The clinics will have a nurse on call in case women develop medical complications. Health officials had argued that abortions past 16 weeks should be performed in a hospital because of the increased risk of possible problems.

It's an important victory in terms of the overall struggle of women," said Robert B. McDuff, one of the attorneys representing the two clinics in Jackson and Southaven.

Nurses at Mississippi Women's Medical Clinic in Jackson and Tri-State Women's Medical Center in Southaven would have access to a physician able to admit women to a local hospital if necessary.

"We are satisfied with these assurances," said Mendal Kemp, director of the Health Facilities Licensure and Certification Division of the State Department of Health.

The agreement settles a lawsuit filed July 28, 1992, by the clinics.

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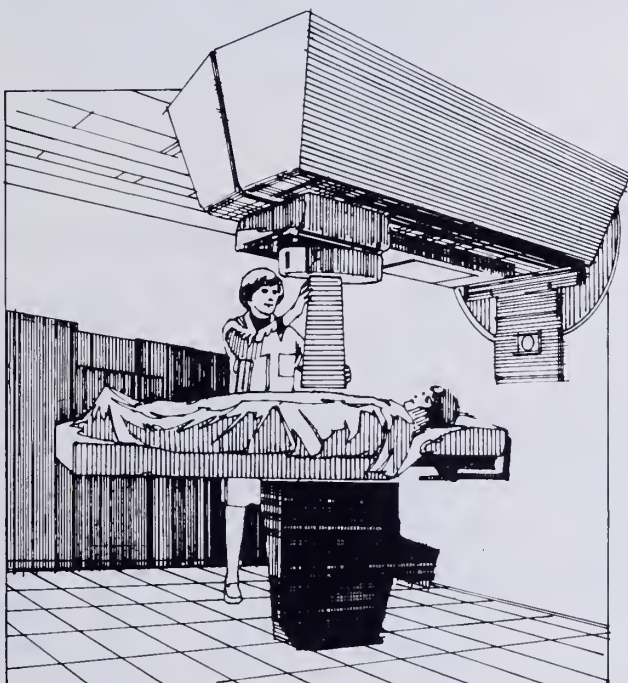
## **Cardiovascular Disease Symposium Scheduled**

Nashville, TN — The First Annual Mid-South Symposium on Cardiovascular Disease will be held July 15-17, 1993, at the Laurence A. Grossman Medical Learning Center, Saint Thomas Hospital, Nashville, Tennessee. This Symposium is sponsored by the American College of Cardiology and is designated at 18.5 CME Credits in Category 1. For information, contact: Registration Secretary, Extramural Programs Department, American College of Cardiology, 9111 Old Georgetown Road, Bethesda, MD 20814-1699; 800-257-4739; Fax 301-897-9745.

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# Aplastic Crisis Due To Human Parvovirus (B19) As An Initial Presentation Of Hereditary Spherocytosis

Gail C. Megason, MD  
J. Clinton Smith, MD, MPH  
Rathi V. Iyer, MD

**A**plastic crisis is an acute, profound anemia without jaundice or reticulocytosis which occurs in individuals with chronic hemolytic anemias. It most commonly occurs in children with sickle cell disease and is due in most instances to infection with human B19 parvovirus. Patients often present as emergencies with weakness, malaise, and striking pallor. The history of chronic hemolytic anemia, the lack of jaundice or splenomegaly, and the potentially life-threatening low hemoglobin level lead the clinician to the correct diagnosis. In the absence of a history of anemia, the diagnosis becomes more elusive. The differential diagnosis would broaden to include sepsis, malignancy, transient erythroblastopenia of childhood, and in a young child possibly congenital red cell anemia.

We present two instances of diagnostic dilemmas in which children were referred to the UMC Pediatric Emergency Room for the evaluation of profound, unexplained anemia.

### Case Report 1

A six year old black male was referred to UMC by his local physician because of a three day history of fever, malaise, abdominal pain, and vomiting. The physician had noted the patient to be severely anemic. There was no history of rash, joint pains, diarrhea, or obvious blood loss. The past medical history was remarkable for an evaluation of anemia and jaundice at age three; hemoglobin electrophoresis at that time was normal. No family history of anemias or other illnesses was elicited. Physical examination revealed a lethargic, very pale, black child with a temperature of 102 degrees F and a pulse of 154/min. There was no icterus, no splenomegaly, and no rash. A complete blood count revealed a hemoglobin of 3.2gm/dl and a hematocrit of 8.9%. The reticulocyte count was 0.6%. The total white blood cell count was 4930/mm<sup>3</sup>, with a platelet count of 172.0 mm<sup>3</sup>. Total bilirubin was 1.8 mgm/dl and the direct coombs was negative. A sickle cell prep was also negative. Chest x-ray re-

vealed an enlarged heart without overt failure. Patient was admitted and transfused to a hemoglobin of 9 gm/dl and discharged home with a reticulocyte count of 1.4% after three days. Review of the initial peripheral smear revealed many microspherocytes. Osmotic fragility was increased. His diagnosis was hereditary spherocytosis.

### Case Report 2

The second patient was a ten year old black male who was referred for evaluation of "low blood counts". He gave a four day history of headaches, fever, and chest and abdominal pain. The patient had no vomiting and only slight diarrhea. He also complained of dizziness and feeling faint. There was no history of rash or joint pain. Past medical history was remarkable for a diagnosis of sickle cell trait at age three when he had been hospitalized for pneumonia. There was no family history of anemias or other illnesses. Physical examination revealed a pallid black boy with a temperature of 96 degrees F and a pulse of 112/min. His liver

was palpable three cms below the right costal margin and the spleen tip was also palpable. No rashes were present, nor was there a heart murmur. A complete blood count revealed a hemoglobin of 3.3 gm/dl, a hematocrit of 8.7%, and a reticulocyte count of 0.3%. Total white cell count was 11,500/mm<sup>3</sup> and platelet count was 304.0mm<sup>3</sup>. Sickie prep was negative. Direct coombs was negative. Hemoglobin electrophoresis revealed Hb AA. Bone marrow aspirate revealed normal cellularity with increased red cell precursors. After admission, the patient was transfused. His peripheral smear subsequently revealed microspherocytes characteristic of hereditary spherocytosis. He was discharged with a hemoglobin of 12.3 gm/dl and a reticulocyte count of 13.0%. A human B19 parvovirus titer was positive for anti-IGM antibodies.

### Discussion

Transient cessation of erythropoiesis in normal subjects is generally well tolerated due to the 120 day life span of the red blood cell. However, in patients with chronic hemolytic anemias and shortened red cell survival, if erythropoiesis is halted then a rapid fall in hemoglobin and hematocrit ensues. This sudden drop in red cell production is termed an aplastic crisis. Aplastic crisis has been reported in patients with sickle cell,<sup>1</sup> thalassemia,<sup>2</sup> hereditary spherocytosis,<sup>3</sup> pyruvate kinase deficiency,<sup>4</sup> elliptocytosis,<sup>5</sup> and G6PD deficiency.<sup>6</sup>

Human parvovirus B19 was first associated with aplastic crisis in 1981.<sup>1</sup> Erythema infectiosum or "fifth" disease was associated with parvovirus in 1983.<sup>7</sup> Epidemiological studies have demonstrated the concurrence of these two entities in an epidemic fashion.<sup>8</sup> B19 parvovirus has also been implicated in some cases of acute arthritis and arthralgias, primarily in adult fe-

male,<sup>9</sup> fetal hydrops,<sup>10,11</sup> the anemia associated with malaria,<sup>12</sup> autoimmune anemia,<sup>13</sup> and the chronic bone marrow failure associated with immunosuppression,<sup>14</sup> leukemia,<sup>15</sup> and bone marrow transplantation.<sup>16</sup> Human parvovirus has a propensity to infect and replicate in erythroid progenitor cells to which it is cytotoxic.<sup>17</sup> The infection is transient, commonly of 7 to 10 days duration, and is terminated by the development of neutralizing antibodies.<sup>18</sup>

In a recent retrospective study at our institution, forty-nine cases of aplastic crisis in children less than eighteen years of age occurred in the five year review period. The majority of cases (73%) were in patients with sickle cell disease, but the second most common diagnosis was hereditary spherocytosis (16%).<sup>19</sup> Due to the severe anemia and the infectious etiology, it is essential that clinicians recognize this entity in order to transfuse and isolate these patients. As can be surmised from our case reports hereditary spherocytosis, or other causes of hemolytic anemia may be previously undiagnosed.

Treatment of an aplastic crisis should consist of judicious transfusion. If it becomes necessary to admit these children to the hospital due to severe anemia and congestive heart failure, they should be carefully monitored. They should be transfused in small increments such as five cc/kg of packed red blood cells over two to four hours. It is also necessary to isolate these children to prevent spread of the viremia to other susceptible patients such as those with sickle cell disease, patients undergoing chemotherapy, and to female caretakers of reproductive age. The risk of fetal hydrops is small but it is nevertheless finite and must be avoided. If hospitalization is not required, education of family members in the signs or symptoms of parvovirus

infection is necessary. Siblings and at least one of the parents may also have hereditary spherocytosis, since inheritance is autosomal dominant. Such family members are also at risk of developing an aplastic crisis.

Human B19 parvovirus is a viral infection which produces many manifestations of illness. For most individuals it is self-limiting and harmless. For patients with underlying hemolytic anemias, it can cause a life-threatening anemia termed an aplastic crisis. For some patients, this crisis may be the presentation of their underlying illness. □

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*Dr. Megason is a resident in Pediatrics, Dr. Smith is Assistant Professor of Preventive Medicine, and Dr. Iyer is Associate Professor of Pediatrics all at the University of Mississippi Medical Center.*



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**CASE RECORDS  
OF THE  
UNIVERSITY OF MISSISSIPPI  
MEDICAL CENTER**

**Clinicopathologic Conference I**

**Selection and Preparation:**

**Todd Adkins, MD**

**Matt Rees, MD**

**Francesco Simeone, MD**

**Joe C. Files, MD, Editor**

**Differential Diagnosis: James L. Achord, MD**

**Radiological Findings: James U. Morano, MD**

**Pathological Findings: Robert J. Peace, MD**

**CASE PRESENTATION**

The patient is a 75 year old white female with a history of hypertension, nephrolithiasis, diverticulosis, glaucoma, chronic sinusitis, and end-stage renal disease who has been on hemodialysis for one year. She was in her usual state of health until four weeks prior to presentation when she developed a painful mass in her left breast and tender nodules over both ankles. The patient complained of anorexia, nausea, vomiting, and generalized weakness, but denied weight loss, fever, and abdominal pain. Three weeks prior the admission an excisional breast biopsy of a 5x5x2 cm lesion was done which showed duct ectasia and chronic inflammation. One of the nodules on the right lower extremity subsequently ulcerated and the patient was treated with a ten day course of intravenous Cefazolin with only mild improvement in the lesions. Ten days and five days prior to admission she received a dose of Vancomycin after hemodialysis, again with minimal improvement. She was subsequently admitted for further evaluation of the lower extremity nodules.

Other significant past medical history includes Staph Aureus septicemia several months prior to admission secondary to an infected Goretex graft and multiple abdominal surgeries for adhesion lysis subsequent to a hysterectomy. The patient also had a history of allergies to penicillin and codeine. Medications on admission included calcium carbonate, so-

dium citrate and vitamins.

On physical examination the patient was an elderly white female who appeared chronically ill but was alert and fully oriented. The left breast wound site was healing well and had no masses, purulence, or induration. She did not have a palpable liver and her abdomen was nontender with no masses palpable. Examination of the extremities revealed violaceous, indurated nodules on both heels which were tender and ranged in size from two to four centimeters. The right shin had a seven centimeter ulcerated lesion which was lymphadenitis. The patient had no focal neurological deficits.

On admission laboratory the WBC was 24,300 with 71% segs and 19% bands. A Chem-7 revealed: Na=140; K=4.4; Cl=98; CO<sub>2</sub>=31; BUN=45; Creat=6.4. A Chem-15 revealed: Ca=9.9; Phos=5.1; Uric Acid=16.4; Alk Phos=156; Alb=3.6; T. Prot=6.9; SGGT=105; SGPT=1500; SGOT=2350 and LDH=4270.

The patient was begun on broad-spectrum intravenous antibiotics and a hepatitis screen was drawn which was positive for Hepatitis A Surface Ab but Hepatitis B studies were negative. The WBC declined over the first few days but there was no improvement in the shin ulcer or nodules. The patient developed several new rapidly expanding nodules over the knee, right hip and left hand. A biopsy of the skin lesions revealed fat necrosis with acute inflammation and abscess formation. Scattered multinucleated Giant cells were noted as well as numerous histiocyte and focal fibroblastic changes. She was treated with local wound care but her condition continued to deteriorate. Four weeks into the hospital course the patient became acutely encephalopathic and developed asterixis.

A study was performed followed by a diagnostic procedure.

**Dr. Achord:** Thank you for asking me to discuss this first in a new series of clinicopathological conferences. Each of you have before you a description of the course of this unfortunate 75 year old woman who was well known to this hospital, having been on dialysis necessitated by renal failure due to hypertension. She also was reported to have nephrolithiasis. She had been treated for staph sepsis from her Goretex graft in the past and had had several abdominal explorations for "adhesions".

Her present illness began some four weeks prior to admission when she had a painful mass in the left breast which, on later biopsy, was reported to be "duct ectasia and chronic inflammation". She developed tender, erythematous nodules over both ankles, some anorexia, nausea and vomiting, and leukocytosis but no fever. Antibiotics were administered without im-



provement. On admission, the nodules were still present and she was afebrile. Her blood pressure and pulse were normal, even though we are told that she was hypertensive in the past. She had several 2-4cm tender, violaceous, indurated nodules on both ankles and a 7cm ulceration of the right pretibial area. The abdomen was soft, there were no abdominal masses and the liver was not enlarged. The remainder of the physical exam was unremarkable. She had a leukocytosis of 24,300 with 21% band forms but no reported eosinophiles. Her electrolytes were normal with minimal elevations of the BUN, phosphorus, and uric acid compatible with her known renal disease. The serum alkaline phosphatase is minimally elevated and is actually in a range that can be called normal in elderly people. Her albumin and globulin were within normal limits, but her AST and ALT were remarkably elevated at 2350 IU/dL, respectively. In addition, we are told that the LDH was markedly elevated. Her prothrombin time (PT) was moderately but significantly elevated at 16 sec.

To digress a moment here, the elevated AST and ALT came somewhat as a surprise. To consider acute viral hepatitis in a 74 year old person is stretching the bounds of observed disease: it is extremely rare, although not unheard of. In the acute care, tertiary hospital such as this one, a very common cause of unexpected and marked elevation of AST and ALT, especially when the LDH is also markedly elevated and the PT is prolonged, is acute ischemic injury to the liver due to low blood flow. Characteristically, the transaminase levels fall to near normal levels in a matter of a few days, as happened in this patient we are told. Other than acute blood loss, sepsis and low perfusion pressures due to endotoxemia is a very common cause. In this case, we cannot rule out sepsis which can also cause skin lesions as we will discuss. Other acute crises, such as acute pancreatitis can also result in low perfusion problems. Unfortunately, for several reasons as we will also see, neither a serum lipase nor amylase was obtained. It is worth pointing out that hypotension does not define shock which is considered to be a state of blood flow that is inadequate to meet metabolic needs; commonly described as low perfusion pressure but not synonymous with peripheral hypotension. In this case, as in all very serious illnesses in which ischemic liver injury is seen, it is an epiphenomenon.

In her hospital course, cultures of blood and of her skin lesions were negative. She developed new skin lesions on the hip and one hand. The lesions became fluctuant and dark yellow fluid was aspirated from them but the fluid is not described further. A biopsy was performed. Dr. Peace, would you describe the

findings for us?

**Dr. Peace:** Regrettably, I'm going to have a run in a look-alike for the skin lesions. The patient's slides were sent to a consultant who retained them. The lesions were just as they were characterized, a necrotizing vasculitis. The lesions are a bit unusual in that the panniculitis was accompanied by a great deal of necrosis and by fatty necrotic changes similar to what you might expect to see in the omentum or fat within the abdominal cavity in pancreatic fat necrosis. The differential diagnosis of the lesions would be that of necrotizing panniculitis and include erythema induratum, a type of panniculitis characterized by extensive involvement of dermal fibrous tissue with necrosis and sloughing onto the surface of the skin, and other forms of panniculitis that are rare. The specific finding here is that this is a type of necrosis of subcutaneous fat and dermal fibrous tissues that perforates the skin and is most characteristic of pancreatic fat necrosis. The lesion in the breast was not relevant to the central problem here. It showed only stomal fibrosis and duct ectasia.

**Dr. Achord:** We now know what the skin lesions were: necrotizing panniculitis. Our job is now simplified into developing a differential diagnosis of panniculitis. However, some time after the biopsy, she became disoriented and asterixis was noted. In a patient in this age group, severe illness of any sort is not uncommonly associated with confusion, but sepsis is still a concern here. Therefore, one must consider brain abscess with or without bacterial meningitis but we have no other neurological findings to suggest that these problems were present; certainly, she was at risk for them. Asterixis is seen in three conditions but usually only searched for in the first of these: namely, liver failure, renal failure, and pulmonary disease with hypoxia. As mentioned, I believe she had acute ischemic liver injury that was typically transient. With normal serum albumin and globulin and no other evidence of liver disease, we would be hard pressed to incriminate that organ. We know she has renal disease but she does not have uremia by definition and she does not have significant pulmonary insufficiency. I cannot explain her asterixis and suspect that her confusion was due to metabolic encephalopathy.

At this point, we have a very sick lady who has necrotizing panniculitis. What does this tell us about her underlying disease process?

Cutaneous ulcerations preceded by subcutaneous painful nodules of relevance here include ecthyma gangrenosum, characteristic of pseudomonas sepsis, and pyoderma gangrenosum, usually associated with



inflammatory bowel disease, some of the dysproteinemias, and rheumatoid arthritis. I believe we can rule out pyoderma for lack of evidence. Ecthyma is still possible, even in the face of negative blood cultures, but the overall clinical picture suggests that sepsis is not the cause of her underlying problem, primarily because she has remained afebrile and we know it has been going on for weeks, not what one would expect in pseudomonas or other sepsis.

The differential diagnosis of necrotizing panniculitis in this setting is limited. It is often categorized in two forms; septal and lobular.<sup>1</sup> In septal panniculitis, inflammation primarily is in the septa between fat lobules whereas lobular panniculitis is characterized by inflammatory cells within fat lobules. Both types can be further defined by the presence or absence of accompanying vasculitis, although this latter point is controversial. Septal panniculitis includes erythema nodosum and subacute migratory panniculitis. It has been described in scleroderma, dermatomyositis, eosinophilic fascitis, and necrobiosis lipoidica diabetorum. Septal panniculitis is sometimes seen in thrombophlebitis and in cutaneous polyarteritis. From the description of the histology as well as the clinical picture, septal panniculitis does not appear to be present.

Lobular panniculitis includes nodular vasculitis and erythema induratum. These problems are not associated with severe systemic disease and do not need to be considered further here.

Lobular panniculitis also includes Weber-Christian disease, following steroid therapy and trauma, and associated with lupus, sarcoidosis, Sweet's disease, systemic infections, lymphoma and leukemia. Although here chronic illness is compatible with lupus, so prevalent in this community, we have nothing to suggest that it is present, and except for systemic infection which we do not believe to be present but which I am reluctant to completely eliminate as a possibility, we are left with one (and the most common) form that probably explains here acute illness; namely, that associated with pancreatic disease.

Acute and chronic pancreatitis as well as carcinoma of the pancreas have been associated with panniculitis and is commonly referred to as "metastatic fat necrosis".

Subcutaneous panniculitis is not a common complication of pancreatic disease but is generally well known by those who treat the disease frequently.<sup>2</sup> The few cases I have seen have been remarkable in that the underlying acute pancreatitis was not accompanied by the characteristic pain associated with that disease. The painful nodules described in this lady are quite compatible with the subcutaneous fat necro-

sis seen in pancreatic disease where there is a release of active enzymes into the circulation. Eosinophilia, not present in our patient, is often present. Liquefaction of stored fat triggers an intense local inflammatory reaction. Resolution of these lesions follows improvement of the pancreatitis, but most clinicians associate subcutaneous fat necrosis with unusually severe disease.

Also associated with pancreatic disease is medullary infarction of bone marrow.<sup>3</sup> That organ is supplied by en-arterioles which, if occluded, results in death of the tissue supplied. Bone marrow infarction is usually asymptomatic and unsuspected but results in characteristic calcification with healing. We reported that a prospective search for bone marrow infarction revealed its presence in about 5% of cases of pancreatitis. We have no radiographs of our patient to tell us if such lesions were present.

What did the chest x-ray show us?

**Dr. Morano:** The admission chest x-ray was performed supine. It showed a few scattered calcific densities throughout the lungs compatible with old healed granulomatous disease. The heart was perhaps borderline enlarged.

**Dr. Achord:** So we don't get much positive help for the chest film. I think this lady has acute painless pancreatitis. As to the risk factors for this disease, the patient was apparently not a user of alcohol and we have no past history suggestive of gallstones (but no current x-rays directed to that point). She may well have had, in addition to ischemic liver disease, pancreatitis on the basis of ischemia, although that would not explain her disease onset some weeks before admission. Carcinoma of the pancreas cannot be ruled out and has been associated with lesion illustrated in this patient.

Given the presence of necrotizing subcutaneous panniculitis, the study indicated and the one probably obtained was computerized tomography of the abdomen or ultrasound with close attention to the pancreas. What was the study obtained?

**Dr. Morano:** We have two images from a CT scan. She had small atrophic kidneys bilaterally which are compatible with chronic renal failure. She also had a small cyst on the left kidney which is common in patients on hemodialysis. The pancreas was visualized and contained no focal masses within it. There were some very poorly defined low density masses in her liver.

On the ultrasound of the abdomen, the liver is seen to have several mass lesions. These lesions are solid,

not cystic. No focal masses were identified in the pancreas by ultrasound but there was a 1cm cystic lesion. The gallbladder was normal.

**Dr. Achord:** So we now have evidence by ultrasound that she has more than one mass lesion in her liver and a very small cystic lesion in her pancreas. These findings suggest malignancy, of course, and with the subcutaneous lesion, pancreatic neoplasm becomes a probable diagnosis. Obviously, a needle biopsy is in order.

**Dr. Peace:** A CT guided biopsy of the liver masses was obtained. A rich harvest of cells was obtained. Even at low power magnification, one can identify cells that are arranged in vague, rather poorly defined acini and in long streams of cells. A Romanowsky type stain reveals malignant neoplasm. It seems to be an adenocarcinoma. We considered a glucagonoma or other endocrine tumor but our special stains were negative. Our final conclusion was that the aspirated tissue represented an adenocarcinoma of the pancreas with metastases to the liver.

The consultant pathologist who examined the skin biopsy was Dr. Donald Leonard and his associate Dr. John Arington, both of whom have a wide reputation in such lesions. They made much in their consultant's report that the skin lesion was necrotizing panniculitis but that it also had most of the characteristics of pancreatic fat necrosis; the recommended evaluation of the pancreas.

#### Diagnosis:

Adenocarcinoma of the pancreas, probably acinar but some features suggested endocrine or neuroendocrine types with metastases to the liver,  
and  
subcutaneous "metastatic" fat necrosis. □

2500 North State Street  
Jackson, MS

#### References:

1. Lazarus GS. Panniculitis and disorders of the subcutaneous fat. In: Wyngaarden JB, and Smith, Jr LH eds. Cecil, Textbook of Medicine, 18th ed. Philadelphia: W.B. Saunders, 1988:2050-2051.
2. DiMagno EP and Clain JE. Chronic pancreatitis. In: Go VL, Gardner JD, Brooks FP, et al, eds. The Exocrine Pancreas. Biology, pathobiology, and diseases. New York: Raven Press, 1986:558-559.
3. Gerle R, Walker L, Achord J, and Weens H. Osseous changes in pancreatitis. Radiology 1965;85:330.

*Dr. Files is Professor of Medicine and Associate Chairman for Clinical Affairs; Dr. Achord is Professor of Medicine; Dr. Morano is Associate Professor of Radiology; and Dr. Peace is Associate Professor of Pathology, all at the University of Mississippi Medical Center.*

*Dr. Adkins, Dr. Rees, and Dr. Simeone were Chief Medicine Residents in the Department of Medicine at the University of Mississippi Medical Center, 1991-92.*



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# Special Article



## OFFICIAL CALL

To: All Members of the Mississippi State Medical Association

The 125th Annual Session of the Mississippi State Medical Association is called to meet in Biloxi, Mississippi on Wednesday, April 28, 1993, pursuant to Article V of the Constitution.

The House of Delegates will be convened at the Royal d'Iberville Hotel at 9:00 a.m. on April 29. The Scientific Assembly will meet April 30 and May 1.

No member or guest will be permitted to participate in any aspect of the Annual Session until regularly registered.

**William C. Gates, Jr., MD, President**

**D. Stanley Hartness, MD, Secretary-Treasurer**

## 125th Annual Session Royal d'Iberville Hotel, Biloxi

MSMA's 125th Annual Session will be held at the Royal d'Iberville Hotel in Biloxi, Mississippi, Wednesday, April 28, - Sunday, May 2, 1993. Individual room reservations should be made directly with the Royal d'Iberville. A room registration form was enclosed in the March *MSMA Report*.

The annual President's Reception will begin, Thursday, April 29, at 6:00 p.m. in the Crystal Room of the hotel. Association members and guest will enjoying music, hors d'oeuvres, and drinks with a tropical flavor. For those who want to try their luck, shuttle buses will be available at 7:30 p.m. for transportation to the Isle of Capri Casino. Buses will run every thirty minutes between the Hotel and Casino until midnight. Dress for the President's Reception is "Tropical" or casual.

The MSMA/MSMA Auxiliary Membership Party will be held, Saturday, May 1, at 6:30 p.m. pool-side at the Royal d'Iberville. This informal evening will include plenty of New Orleans Jazz and Cajun food. Dress is casual.

The MSMA Auxiliary will once again hold a silent auction with proceeds benefiting AMA-ERF. Association members and guest will have the opportunity to browse through the items for auction and place their silent bid during the party.

## House of Delegates

The opening session of the House of Delegates

will convene on Thursday, April 29, at 9:00 a.m. Speaker of the House Dr. Vann Craig of Natchez requests that all delegates be certified and in place at 9:00 a.m.

Delegates will hear an address by Dr. Daniel H. Johnson, Jr., AMA Speaker, House of Delegates. Dr. William C. Gates, Jr., MSMA president will also address the House.

Reports and resolutions will be introduced at the initial meeting of the House for consideration by Reference Committees which will meet on Thursday and Friday afternoons. The MSMA 1993 Community Service and other special awards will be presented during the opening session.

Delegates will reconvene on Sunday morning, May 2, to take action on policy recommendations and to elect MSMA officers for 1993-94. The installation of Dr. Don Q. Mitchell, of Jackson as MSMA 1993-94 president will mark the official conclusion of the 125th Annual Session.

## Hospital Medical Staff Section • Young Physician Section Joint Meeting

MSMA's Hospital Medical Staff Section (HMSS) and Young Physician Section (YPS) will host a joint session which is open to all annual session participants.

This session will be held on Thursday, April 29, at 2:00 p.m. The HMSS and YPS will meet separately for their individual business sessions at 3:30 pm.



# **125th Annual Session**

## **Summary of Daily Events**

### **WEDNESDAY, APRIL 28**

Technical Exhibit Set-up  
Scientific Exhibit Set-up  
MSMA Registration Opens

### **THURSDAY, APRIL 29**

Continental Breakfast - Exhibit Area  
House of Delegates  
Women In Medicine  
MS Foundation for Medical Care  
Annual Meeting  
Reference Committee  
HMSS/YPS Joint Meeting  
HMSS/YPS Section Meetings  
MFMC Review Physicians Meeting  
President's Reception

### **FRIDAY, APRIL 30**

Continental Breakfast - Exhibit Hall  
Medicine Plenary Session  
MSMA Auxiliary House of Delegates  
MS EENT Association  
MS Association of Public Health Physicians  
MS Academy of Family Physicians  
MS Society of Internal Medicine  
MS Chapter, American Academy of Pediatrics  
MS Psychiatric Association  
Reference Committee Meetings  
Medical Alumni Functions

### **SATURDAY, MAY 1**

Surgery Plenary Session  
Fifty-Year Club  
Cancer Liaison Physicians  
MS Chapter, American College of Surgeons  
MS Society of Anesthesiologists  
MS Dermatological Society  
MS Chapter, Emergency Physicians  
MS Association of Pathologists  
MS Nephrological Society  
MSMA/MSMAA Membership Party

### **SUNDAY, MAY 2**

Protestant Services  
House of Delegates

## **Scientific Programs**

The Medicine and Surgery Plenary Sessions are Scheduled for Friday, April 30 and Saturday, May 1. Both sessions will address the current issues of Health System Reform. Members are encouraged to attend both plenary sessions.

The Council on Scientific Assembly designates this continuing medical education activity for 11 hours of Category 1 of the Physicians Recognition Award of the American Medical Association. (Medicine plenary Session - 4 hours; Surgery Plenary Session - 7 hours)

Individual programs for the Medicine and Surgery plenary sessions will indicate the designated CME hours for each session. Participants should keep each program for their CME attendance records.

## **Technical Exhibits**

The Technical Exhibit features 65 displays of the latest in resources for physicians. The program includes two continental breakfasts and one luncheon in the exhibit area. This was planned to provide MSMA members with additional opportunities to view the exhibits and talk with the professional representatives who will be available to provide information. Members are eligible for numerous exhibit registration awards.

## **MSMA Auxiliary**

The MSMA Auxiliary will be conducting their 70th Annual Session during the week.

MSMA and MSMA Auxiliary members will again have the opportunity to enjoy coffee, soft drinks, and homemade refreshments in the Auxiliary's Hospitality Center located in the hotel's first floor lobby.

The MSMA Auxiliary will hold a silent auction during the Membership Party on Saturday evening, May 1. The proceeds from this auction will benefit the AMA ERF.

## **Recreational Activities**

The Annual Golf Tournament will be held Saturday, May 1, at noon on the Broadwater Sun Course. The Tennis Tournament will also be held at noon Saturday, May 1, at the Gulfport Racquet Club.

The Annual Fishing Rodeo will be held on Friday, April 30 and Saturday, May 1.

Pre-registration is required for all tournaments.

## SCIENTIFIC PROGRAMS

# Health Care Reform... Challenges and Opportunities

### Friday, April 30

### Medicine Plenary Session

- 8:00 AM *New Drugs 1993*  
Tom Frank, MD, Jonesboro Arkansas
- 8:45 AM *HIV Disease in Mississippi*  
Bill Causey, MD
- Current Public Health Issues*  
Ed Thompson, MD
- 10:00 AM *The Administration's Plans for Health Care Reform*  
A representative from the Health Care Reform Task Force
- Implementing Managed Competition*  
C. J. Bolster, Peat. Marwick, Mitchell
- The HMO View of Managed Competition*  
Howard Waltman, SANUS Corporation Health System
- Noon *Adjourn*

### Saturday, May 1

### Surgery Plenary Session

- 8:00 AM *J. T. Davis Hand Lecture*
- 9:00 AM *State Health Care Reform Strategies*  
John E. Patchett, JD, Director, AMA Department of State  
Legislation
- Medicaid... Its Present and Future*  
Helen Wetherbee, Director, MS Division of Medicaid
- Quality of Care/Outcomes Measurement*  
Alton B. Cobb, MD, MFMC
- Alternative Dispute Mechanisms*  
Andy Warshaw, MD, Chief of General Surgery,  
Massachusetts General
- Noon *Plenary Session Adjourns*
- ACS Luncheon*
- 1:30 PM *Surgery of the Pancreas*  
Andy Warshaw, MD, Chief of General Surgery,  
Massachusetts General
- 2:30 PM *Trauma Research Papers*  
UMC Residents
- 3:00 PM *Adjourn*

# TECHNICAL EXHIBIT MSMA 125th Annual Session

**Royal d'Iberville Hotel  
Biloxi, MS  
April 29 - 30, 1993**

Exhibitor	Booth	Exhibitor	Booth
Abbey Home Healthcare .....	52	Miles, Inc .....	42
Abbott Laboratories .....	31 & 32	MS Army National Guard .....	38
Abraham Medical-Dental .....	63	MS Baptist Chemical Dependency Center .....	27
Adams Labs .....	4	MS Foundation for Medical Care .....	20
AMGEN .....	30	MS Methodist Rehabilitation Center .....	41
Automated Health Systems, Inc .....	33	MS Physicians Insurance Company, Inc. ....	19
Ayerst .....	37	MS State Department of Health .....	26
Ballard Medical Imaging, Inc .....	61	MSMA Benefit Plan & Trust .....	18
Bedsole Medical Companies, Inc .....	53	Parke-Davis .....	59
BFI Medical Waste Systems .....	28	Pfizer Labs .....	39
Charter Hospital of Jackson .....	36	Pine Grove Recovery Center .....	24
CIBA Pharmaceuticals .....	56	Puckett Laboratory .....	55
Coastal Emergency Services of Memphis, Inc. ....	15	River Bay Corporation .....	23
Complete Medical Systems, Inc .....	64	Roche Laboratories .....	12
Corporate Planning, Ltd. ....	60	Salcris Systems .....	14
CSC Healthcare Systems .....	58	Sandoz Pharmaceuticals .....	25
Doctors Insurance Reciprocal .....	10	Schwarz Pharma .....	3
DP Associates, Inc. ....	51	SmithKline Beecham Pharmaceuticals .....	50
Encyclopaedia Britannica, North America .....	34	Southern Medical Association .....	35
Express Claim Processing .....	1	Sta-Home Health Agency .....	44
Geigy Pharmaceuticals .....	57	The Doctors Company .....	49
Healthcare Economics .....	65	The P.I.E. Mutual Insurance Company .....	40
Healthcare Suppliers, Inc. ....	45	The Trusty Company, Inc .....	21
IC System .....	46	The Upjohn Company .....	62
Independent Computer Service .....	47	Travelers Medicare .....	29
Insurance Corporation of America .....	13	United States Air Force .....	22
Key Pharmaceuticals .....	48	United States Army Medical Department .....	11
MeadJohnson Pharmaceuticals .....	43	Vital Care, Inc .....	2
Medical Assurance Company of MS .....	17	Weight Watchers in Greater MS .....	16
Medical Pathology Laboratory, Ltd. ....	54		





# **Mississippi State Medical Association Auxiliary**

**70th Annual Session  
April 28 - May 2, 1993  
Royal d'Iberville Hotel  
Biloxi, MS**

## **WEDNESDAY, APRIL 28**

3:00 PM - 5:00 PM

Registration - Main Lobby

## **THURSDAY, APRIL 29**

8:00 AM - 4:00 PM

Registration - Main Lobby

10:00 AM - 4:00 PM

Hospitality Center

11:00 AM

Pre-convention Board Meeting & Luncheon

Room B - \$10.00

1:30 PM

Docent guided tour of the Walter Anderson Museum &

Afternoon Tea - \$10.00

6:00 PM - 8:00 PM

MSMA President's Reception

## **FRIDAY, APRIL 30**

8:00 AM - 12:00 PM

Registration - Main Lobby

9:00 AM

House of Delegates Continental Breakfast  
& Meeting

12:00 AM

MSMA Auxiliary Luncheon - \$15.00

2:00 PM - 4:00 PM

Hospitality Center - Main Lobby

2:30 PM

Post-convention Board Meeting

## **SATURDAY, MAY 1**

8:00 AM

MSMAA Past Presidents' Breakfast

10:30 AM

Brunch and tour of the historic home of

Dr. & Mrs. Harry Danielson, hosted by Gulfport Auxiliary

6:30 PM

MSMA & MSMAA Membership Party



## The President's Page

WILLIAM C. GATES, MD

### Reform Revisited

**"These times of ours are serious and full of calamity." — Emerson**

**H**ow often lately have you heard more and more of your colleagues describing organized medicine (the "AMA" in particular) in the following ways: "*They don't represent me...*" or "*What have they ever done for me?*". It seems to me that the frequency and the intensity of these and similar remarks are on the rise and appear coincidental with the frustration and anxiety over the unknowns of health care system reform. Every time we fall into the "circle the wagons and shoot inward" philosophy trap, we delight our detractors with our divisive dialogue and reinforce the old adage, "We don't have to worry about the doctors sticking together," and they don't. Why can we not understand and utilize the admonition, "Ask not what your profession can do for you, but what you can do for your profession," to paraphrase the late John F. Kennedy (and one of our MSMA past presidents, Joe Burnett). There is no question in my mind that *unity* has never been more critical for American medicine than now.

The dictionary defines unity as "a being united - oneness; a single separate thing; harmony, agreement; a harmonious, unified arrangement of parts; continuity of purpose and action." Unity could convert concern into a cause, anxiety into action and worry into productive work by the focusing of the emotion and harnessing of the energy generated by the prospect of change and all the potential perils that come along with it. The messages from organized medicine *must* be *united* in order to be effective. We can be a formidable force, willing to recognize the inevitability of change and ready to work to shape change for the better.

I think we can all agree that change is clearly needed. However, neither unrestrained competition nor increased regulation will benefit us or our patients. Neither approach fully grasps what is unique about quality medical care in the U.S. Unrestrained competition forces behavior more like entrepreneurs and less like medical professionals.

(Continued on page 122)

## Waiting For The Windfall

I expect that by now most physicians have heard of the expected "windfall" in income promised by President Clinton, and generated by the current secret commission formulating changes in the health care system in the United States. In fact he stated that the "windfall" was to be so great that he was also recommending institution of a six percent surcharge on the gross earnings of physicians and other health care providers. This is strange rhetoric considering all the reports regarding cutting of fees, limiting services, managed care and a multitude of other changes. For some reason I fail to see any evidence of a "windfall" on the horizon. Is it all to come from the thirty seven million currently uninsured who will be insured by the new program? Will their benefits be at some higher level and more than compensate for proposed reductions to the extent that a surtax is needed? Well, don't hold your breath waiting for that to be the case.

The dictionary gives four definitions for "windfall". The first is: "an unexpected legacy or an unexpected piece of good fortune". Legacy is defined as "a bequest of property or money" or "something coming from our ancestors or predecessors". Something like this was not unexpected and one would not consider the addition of a surtax as a gift, but we do not think like politicians.

The real worry is that a secret commission was needed to develop this piece of good fortune. I do not recall any situation where a politician found it necessary to keep good news a secret, as they are always very anxious to have all good political fortunes well publicized. This also tells me something.

The next three definitions of "windfall" are more literal: 1 - "something blown down by the wind, as fruit from a tree, or a number of trees in the forest"; 2 - "the tract of fallen trees and the like which indicate the path of a tornado"; 3 - "a violent gust of wind reaching from coastal ranges and mountains to the sea". The Clinton proposals will surely be like a violent gust of wind speeding from Washington across the country.

The word following "windfall" in the dictionary is "windfallen" which is defined as "blown down by the wind". I expect the medical fields and forests of this country will be littered by the "windfallen" generated by the proposed "windfall" and the accompanying surtax. The big question is; what major changes, sacrifices and re-education will be required to avoid being one of the "windfallen" in the current storm of health care proposals?

Myron W. Lockey, MD  
Editor

The editorial opinions expressed in this Journal are those of the indicated author. Editorial opinions are not expressions of the views, or official policies of The Mississippi State Medical Association. We encourage the membership to submit letters for publication regarding any opinion expressed or information contained in the Journal.



## President's Page

(Continued from page 120)

Increased regulation erodes the privacy and autonomy at the heart of the physician-patient relationship. We must be united in the common purpose of insisting that these distinctive qualities of our profession are not forfeited.

The medical profession sometimes disagrees about what precisely is the right course to take for health care reform but what we have in common far exceeds our differences. I feel certain we could all agree on the following as regards to change in the health care system:

- it must assure defined health care coverage to all Americans.
- it must preserve our patients' right to freely choose their own physicians and health care system.
- it must defend the right of patients with their physicians to decide on their medical care, without outside interference and burdensome administrative costs.
- it must decisively promote professional liability reform.
- it must work to moderate the causes of spiraling costs through outcomes research, practice parameters, reasonable aspects of managed care, preventive care, sharing information, elimination of self-referral and unnecessary care and fraud and corruption.

- it must ensure fair negotiation over managed care, insurance industry reform and reasonable reimbursement for Medicare and Medicaid to prevent cost-shifting.

Although nearly all Americans receive medical care when they need it, too many are uncertain about how to get adequate care on a regular basis, how to pay for it and how to keep coverage

if they change or lose their jobs. This is no longer acceptable to the medical profession or to the American public.

"There is nothing more difficult to take in hand, more perilous to conduct or more uncertain in its success than to take the lead in the introduction of a new order of things." Those are the words of Nicolo Machiavelli in *The Prince*. The words ring true in describing the ethical and economic crisis in which we find our profession at this point in history. The crisis is complex, cataclysmic in its proportions and will precipitate a national dialogue and debate, the dimensions of which will be unequaled in the foreseeable future.

The time has come - you are going to have to decide how you feel, what you want done, who is going to do it, how it is going to get done and who is going to pay for it. You will have to choose among standing shoulder-to-shoulder with your colleagues united in mind and purpose or hiding on the fringe in the shadows of the la-la land of indecision and waffling or up in the hills far away firing pot-shots of criticism at the whole process knowing full well that you are safely removed from accountability. The second category is damaging but the third is destructive in a very malignant sense. Thomas Carlyle said, "Nothing is more terrible than activity without insight." What category do you wish to place yourself in - and which group would you like to see your friends and associates choose? The strength of the wolf is in the pack - the strength of the pack is in the wolf. Unity is indeed power and without power our mission will fail in this time of crisis.

The Chinese word for "crisis" is composed of two picture char-

acters... one means "danger" and the other means "opportunity." This crisis is an opportunity for each of us as members of organized medicine to get invested, get informed and get involved in our personal and professional futures.

"These times of ours are serious and full of calamity. But all times are essentially alike. As soon as there is life, there is danger." Emerson said that. But he also said, "This time, like all times, is a very *good* one, if we but know what to do with it."

I hope my letter finds you and yours doing well...

Best regards,  
Bill

## COMMENTS or QUERIES....

The Editors of *Journal MSMA* invite you to comment on any material that appears in or is absent from the publication.

If you have a query or comment, please send it to:

The Editor,  
*Journal MSMA*,  
PO Box 5229,  
Jackson, MS  
39296-5229

# "Current Opinions"

of the Council on Ethical and  
Judicial Affairs of the American  
Medical Association

## Opinions on Professional Rights and Responsibilities

### DUE PROCESS

The basic principles of a fair and objective hearing should always be accorded to the physician whose professional conduct is being reviewed. The fundamental aspects of a fair hearing are: a listing of specific charges, adequate notice of the right of a hearing, the opportunity to be present and to rebut the evidence, and the opportunity to present a defense. These principles apply when the hearing body is a medical society tribunal or a hospital committee composed of physicians.

These principles of fair play apply in all disciplinary hearings and in any other type of hearing in which the physicians may be deprived of valuable property rights. Whenever physicians sit in judgement on physicians and whenever that judgement affects a physician's reputation, professional status, or livelihood, these principles of fair play must be observed.

All physicians are urged to observe diligently these fundamental safeguards of due process whenever they are called upon to serve on a committee which will pass judgement on physicians. Medical societies and hospital medical staffs are urged to review the constitution and bylaws of the society or hospital medical staff to make sure that these instruments provide for such procedural safeguards. □

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**Contraindications:** Renal diseases, and patient's sensitive to the drug. In view of the limited and inadequate information at hand, no precise tabulation can be offered of additional contraindications.

**Warning:** Generally, this drug is not proposed for use in females and certainly must not be used during pregnancy. Neither is this drug proposed for use in pediatric, geriatric or cardio-renal patients with gastric or duodenal ulcer history. Nor should it be used in conjunction with mood-modifying drugs such as antidepressants, or in psychiatric patients in general.

**Adverse Reactions:** Yohimbine readily penetrates the (CNS) and produces a complex pattern of responses in lower doses than required to produce peripheral a-adrenergic blockade. These include, anti-diuresis, a general picture of central excitation including elevation of blood pressure and heart rate, increased motor activity, irritability and tremor. Sweating, nausea and vomiting are common after parenteral administration of the drug.<sup>1,2</sup> Also dizziness, headache, skin flushing reported when used orally.<sup>1,3</sup>

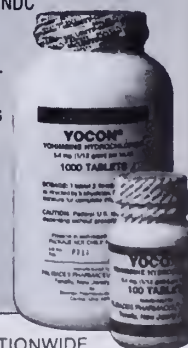
**Dosage and Administration:** Experimental dosage reported in treatment of erectile impotence.<sup>1,3,4</sup> 1 tablet (5.4 mg) 3 times a day, to adult males taken orally. Occasional side effects reported with this dosage are nausea, dizziness or nervousness. In the event of side effects dosage to be reduced to 1/2 tablet 3 times a day, followed by gradual increases to 1 tablet 3 times a day. Reported therapy not more than 10 weeks.<sup>3</sup>

**How Supplied:** Oral tablets of Yocon<sup>®</sup> 1/12 gr. 5.4 mg in bottles of 100's NDC 53159-001-01 and 1000's NDC 53159-001-10.

#### References:

1. A. Morales et al., New England Journal of Medicine: 1221. November 12, 1981.
2. Goodman, Gilman — The Pharmacological basis of Therapeutics 6th ed., p. 176-188. McMillan December Rev. 1/85.
3. Weekly Urological Clinical letter, 27:2, July 4, 1983.
4. A. Morales et al., The Journal of Urology 128: 45-47, 1982.

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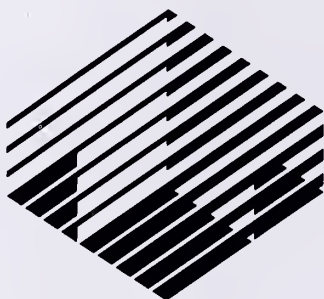


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# Medical Organization

## Dr. "C.D." Taylor, A Long Time Coast Physician Dies

Dr. Charles Daniel "C.D." Taylor, Jr., 73, of Pass Christian died Thursday, February 23.

Dr. Taylor, a native of New Orleans, was a retired family physician. He was a former member of the Board of Trustees of the Mississippi State Medical Association for 13 years serving as secretary, vice chairman and chairman of the Board. Dr. Taylor was also Speaker of the House of Delegates of the Association and a delegate to the AMA. He was a former president of Tulane Medical Alumni.

A member of Pass Christian Rotary Club, Dr. Taylor had served as president, a Paul Harris Fellow and a trustee of the Charity Trust. He was a Knight of the Order of St. Lazarus of Jerusalem and State Commander of Mississippi and a member of the Boston Club in New Orleans.

He served as director of the State Chapter of the American Academy of General Practice and Gulf Coast Clinical Society and was past president of the Coast Counties Medical Society.

Dr. Taylor served in the Navy during World War II. He was active in the Boy Scouts of America. Dr. Taylor was president of the Pass Christian Historical Society, served as Com-

modore of the Pass Christian Yacht club and was an adviser and director of Hancock Bank. He was also vestryman for Trinity Episcopal church in Pass Christian and chairman of the building fund.

Dr. Taylor was selected Pass Christian's Outstanding Citizen in 1965. He received the Laurel Wreath Award in 1970, and was selected Mississippi's Family Physician of the Year in 1985.

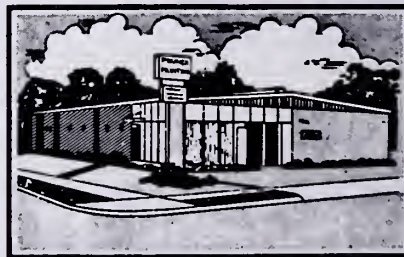
He had served on the staff at Memorial Hospital at Gulfport

since 1948 and was chief of staff, co-chairman of the MHG Building Committee and MHG Planning Committee and a Board member of the MHG Development Foundation. Dr. Taylor was the recipient of the Donald Evans Sutter award for service to Memorial Hospital at Gulfport.

Memorial may be made to the MHG Development Fund, Trinity Episcopal Church Building Fund or the Pass Christian Historical Society. □

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# Dr. Authur Aaron Derrick, Jr., MSMA Past President Dies

Dr. Authur Aaron Derrick, 73, died in Montfort Jones Hospital Saturday, March 6, of injuries received in an automobile accident on Mississippi 35 North.

A native of Goodman, Dr. Derrick was a graduate of Holmes County Agricultural High School and the University of Tennessee College of Medicine. He also attended the University of Mississippi, pledging to the Phi Kappa Alpha fra-

ternity. In 1941, he became a house doctor at the former Charity Hospital in Jackson.

Dr. Derrick volunteered for military service after Pearl Harbor, reported to Greenville Air Force Base in July 1942, and was assigned to service at Starkville Glider School. He was sent to England as a squadron flight surgeon and returned to the United States in September 1945, when he became assistant superintendent of the Charity Hospital in Natchez.

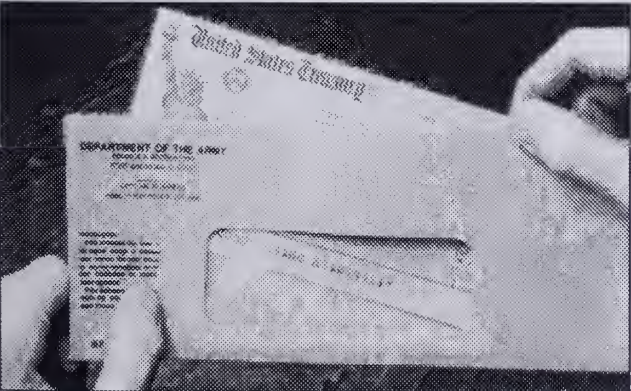
In April 1946, Dr. Derrick came to Durant to practice medicine close to home and served the town for 44 years.

In 1973, Dr. Derrick was elected president of the Mississippi State Medical Association. He served as a member of the association's board of trustees from 1974 to 1980 and as board chairman from 1979 to 1980. He served on the board of the Mississippi Foundation for Medical Care (MFMC), on the Risk Management Committee of the Medical Assurance Company of Mississippi (MACM), and was chief of staff of District II Community Hospital since 1950.

Memorials may be made to the University of Mississippi Library in Oxford. □

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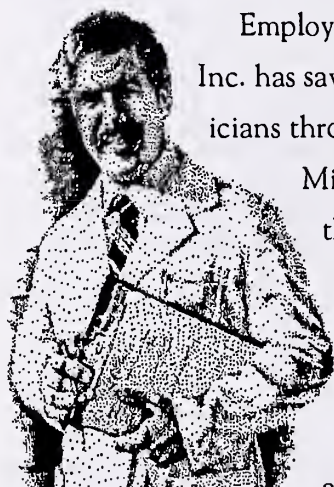
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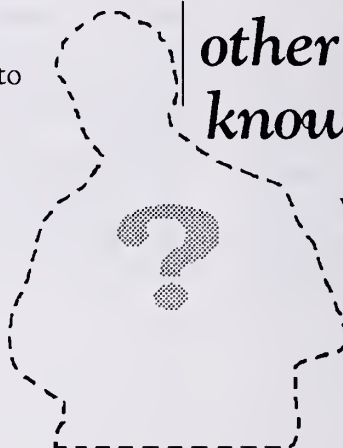
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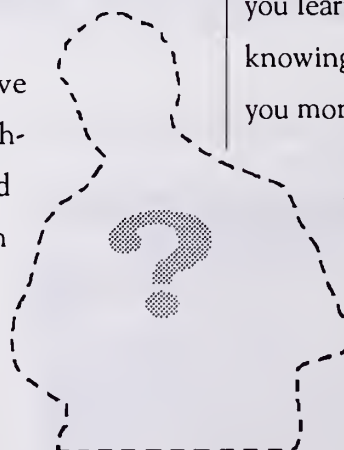
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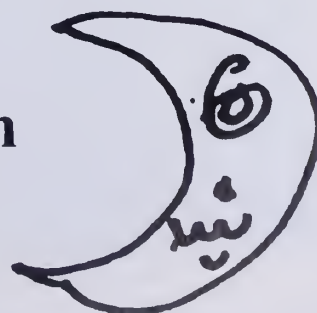
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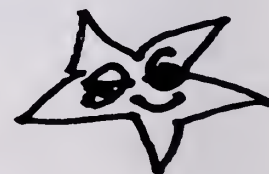
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# New Members

**Barbee, W. Ralph**, Corinth. Born Memphis, TN, April 7, 1936; MD, University of Tennessee College of Medicine, Memphis, TN, 1961; interned one year DC General Hospital, Washington, DC; Dermatology residency St. Lukes Hospital & Columbia Presbyterian Hospital, New York City, NY, 1963-69; elected by Northeast Mississippi Medical Society.

**Crompton, John D.**, Starkville. Born Ashville, NC, July 1, 1960; MD, University of North Carolina School of Medicine, Chapel Hill, NC, 1986; interned one year Bowman Gray School of Medicine, Winston Salem, NC; orthopaedic surgery residency, same, 1987-91 and hand surgery residency, University of Florida School of Medicine, Miami, FL, 91-92; elected by Prairie Medical Society.

**Doorenbos, David I.**, Jackson. Born Baltimore, MD, August 26, 1960; MD, University of Mississippi School of Medicine, Jackson, MS, 1987; interned and neurology residency University Medical Center, Jackson, MS, 1987-91; elected by Central Medical Society.

**Horowitz, Michael D.**, Pascagoula. Born Jersey City, NJ, December 1, 1954; MD, University of Miami School of Medicine, Miami, FL, 1981; surgery residency, same, 1981-86; thoracic and cardiovascular surgery residency,

Ochsner Medical Foundation, New Orleans, LA, 1986-88; elected by Singing River Medical Society.

**Jones, Dan**, Jackson. Born Morton, MS, March 19, 1949; MD, University of Mississippi School of Medicine, Jackson, MS, 1975; interned and medicine residency, University Medical Center, Jackson, MS, 1975-78; elected by Central Medical Society.

**McKibben, Everett C.**, Starkville. Born Starkville, MS, March 9, 1963; MD, University of Mississippi School of Medicine, Jackson, MS, 1989; family practice residency, Alabama Medical Center, Tuscaloosa, AL, 1989-92; elected by Prairie Medical Society.

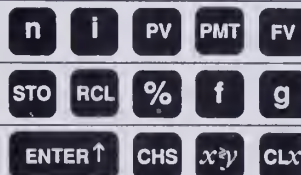
**Nix, R. L.**, Winona. Born Monticello, MS, July 22, 1933; MD, University of Mississippi School

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of Medicine, Jackson, MS, 1958; interned one year, University Medical Center, Jackson, MS, elected by North Central Medical Society.

**Soucie, Pierre F.**, Columbia. Born Canada, July 29, 1959; MD, University of Ottawa School of Medicine, Canada 1985; residency in family medicine and emergency medicine McGill University in Montreal, Canada 1985-88; elected by South Mississippi Medical Society.

**Stefani, Anne M.**, Hattiesburg. Born Syracuse, NY, July 18, 1961; MD, University of Mississippi School of Medicine, Jackson, MS, 1989; family practice residency, UMC, Jackson, MS, 1989-92; elected by South Mississippi Medical Society.

**Stogner, Steven W.**, Hattiesburg. Born Tylertown, MS, June 19, 1960; MD, University of Mississippi School of Medicine, Jackson, MS, 1986; interned and internal medicine residency, UMC, Jackson, MS, 1986-89; fellowship in critical care medicine, Louisiana State Univ. Medical Center, New Orleans, LA, 1989-90 and fellowship in pulmonary diseases, same, 1990-92; elected by South Mississippi Medical Society.

**Stokes, J. Michael**, Carrollton. Born Chicago, IL, Feb. 9, 1955; MD, University of Health Sciences College of Osteopathic Medicine, Kansas, MO, 1985; interned one year Oklahoma Osteopathic Hospital, one year; and medicine residency, St Luk's Hospital, Kansas City, MO, 1986-89; elected by North Central Medical Society.

**Thompson, Anne R.**, Jackson. Born Little Rock, AR, June 9, 1958; MD, University of Arkansas School of Medicine, Little Rock, AR, 1984; interned and surgery residency

University of Louisville, Louisville, KY, 7/84 - 12/87 and 7/89 - 12/91; endocrine research fellowship, Mass. General Hospital, Boston, MA, 1/88 - 6/89; elected by Central Medical Society.

**Young, W. Daniel**, Waynesboro. Born Missouri, Jan 7, 1937; MD, University of Mississippi School of Medicine, Jackson, MS, 1962; interned Oakland Naval Hospital, Oakland, CA, one year 1963; surgery residency, same, 1963-68; elected by South Mississippi Medical Society. □

## Deaths

**Crull, Luther P.**, Winona. Born in Greenwood, MS, September. 4, 1912; MD, Tulane School of Medicine, New Orleans, LA, 1940; interned Charity Hospital, New Orleans, LA, one year; surgery residency one year, Same; Died February 22, 1993, age 80.

**Tyler, Charles C.**, Collins. Born Picayune, MS, May, 21, 1929; MD, Tulane University Medical School, New Orleans, LA, 1954; interned Baptist Hospital Nashville, TN, one year; died Dec. 11, 1992, age 63. □

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## Personals

**Thomas Adams**, a pediatrician in Columbus has recently been elected president of the Prairie Medical Society.

**William G. Bush and William K. Sutherland** announce the formation of Bush-Sutherland OB-GYN, PA, 1020 River Oaks Drive, Suite 100, Jackson.

**Richard M. Glasgow**, and **William A. Spencer** announce the opening of North Mississippi Family Medicine Group, 1397 Belk Blvd, Oxford.

**B. Thomas Jeffcoat**, and **William H. Meyer** have associated with King's Daughters Hospital in the practice of orthopaedic surgery, Brookhaven.

**W. Thomas McCraney, Jr.**, has associated with Capital Orthopaedic Clinic, PA, in the practice of orthopaedic surgery, 971 Lakeland Drive, Suite 315, St. Dominic Medical Offices, East Tower, Jackson.

**William M. McKell, Jr.**, announces the relocation of his office for the practice of internal medicine and gastroenterology to 4105

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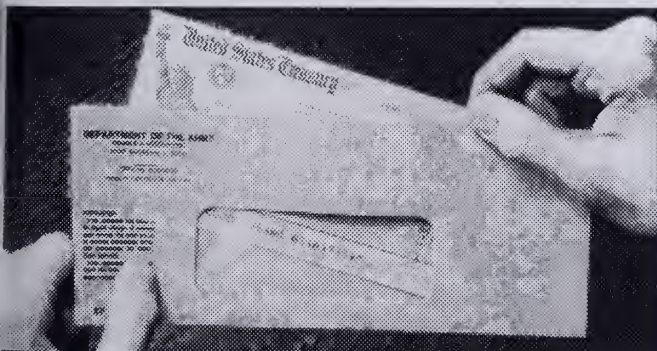
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# Physicians' Recognition



Four MSMA members were named recipients of the AMA Physicians Recognition Award in February 1993. This award is presented by the American Medical Association to Physicians who have voluntarily completed a specified number of continuing medical education hours. These individuals are presented below by Medical Society.

CENTRAL MEDICAL SOCIETY  
**C. Ralph Daniel, III, MD**  
**Richard E. Rhoden, MD**

COAST COUNTIES MEDICAL SOCIETY  
**Eric J. Wyble, MD**

SOUTH MISSISSIPPI MEDICAL SOCIETY  
**Clyde R. Allen, MD**

## Personals/continued

Hospital Road, Medical Arts Building, Suite 111, Pascagoula.

**Beverly A. McMillan, Freda McKissic Bush and Donna G. Breeland** announce the formation of East Lakeland OB-GYN Associates, PA, 1020 River Oaks Drive, Suite 320, Jackson.

**Francis Morrison** of Jackson, was re-elected President of the Board of Trustees of the SCABB Foundation. The Foundation Trustees are responsible for collecting and overseeing funds for grants to be used for education related to Transfusion Medicine within the South Central District.

**James R. Thompson** of Jackson won first place in the section on Emergency Medicine division of Southern Medical Association's 1992 Physicians'-In-Training competition for his scientific research paper *Evaluation and Treatment Modalities for Rhinocerebral Mucormycosis in an Immune Compromised Murine Model*.

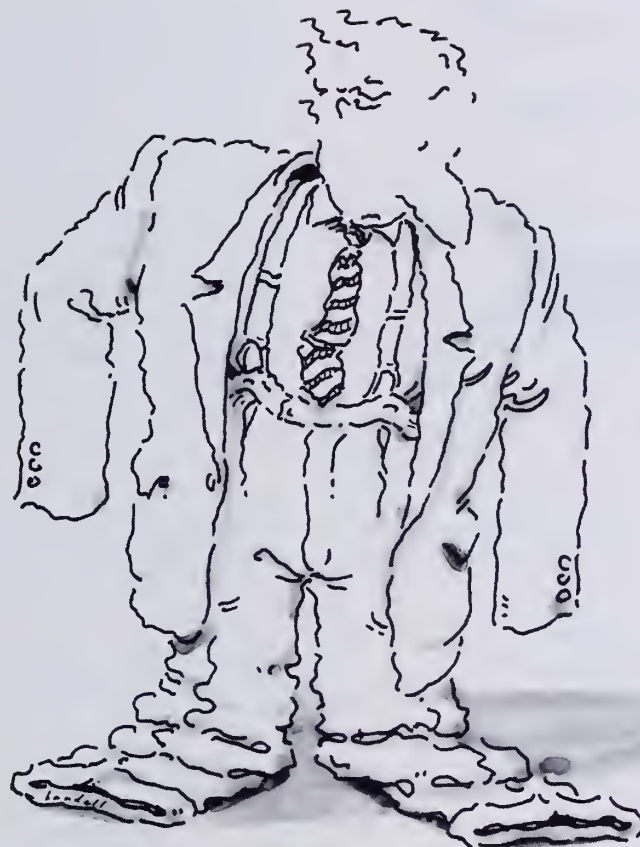
**Schedell Walley** of Waynesboro has joined the staff of Jasper Medical Services in Heidelberg.

**James E. Warrington** of Clarksdale has completed continuing medical education requirements to retain active membership in the American Academy of Family Physicians.

**Chris E. Wiggins**, of Pascagoula has been accepted into the American College of Occupational and Environmental Medicine. □

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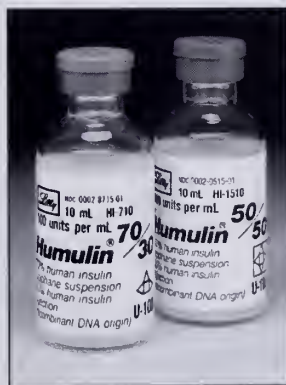





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**Emergency room physicians wanted.** Six hospital contracts in northeast Mississippi. Salary ranges \$90,000 to \$150,000 plus health insurance, life insurance, malpractice insurance, moving expenses. Call (601) 328-8385.

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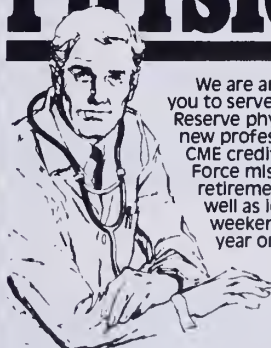
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## Index to Advertisers

Bristol-Myers Squibb Company - Pravachol .....	third and fourth cover
CancerPay Plus .....	7
Central Medical Auxiliary .....	129-132
CompHealth .....	114
Disability Determination .....	138
Eli Lilly & Co. - Humulin .....	137
Employer Plus, Inc. ....	128
Medical Assurance Co. of MS .....	124
Medley & Company .....	133
MS Emergency Association .....	138
MS Methodist Rehabilitation Ctr. ....	second cover
MS Physicians Insurance Company .....	8
MSMA Benefit Plan & Trust .....	110
Palisades Pharmaceuticals, Inc. - Yocon .....	123
Premier Printing .....	126
PRI-MED, Inc. ....	134
The Doctors' Company .....	4
Trustmark .....	125
US Air Force .....	109
US Air Force Reserve .....	139
US Army Active .....	135
US Army Reserve .....	127



**Reference:** 1. Jones PH, et al. Once-daily pravastatin in patients with primary hypercholesterolemia: a dose-response study. *Clin Cardiol*. 1991;14:146-151.

## PRAVACHOL® (Pravastatin Sodium Tablets)

### CONTRAINDICATIONS

Hypersensitivity to any component of this medication.

Active liver disease or unexplained, persistent elevations in liver function tests (see WARNINGS).

**Pregnancy and Lactation.** Atherosclerosis is a chronic process and discontinuation of lipid-lowering drugs during pregnancy should have little impact on the outcome of long-term therapy of primary hypercholesterolemia. Cholesterol and other products of cholesterol biosynthesis are essential components for fetal development (including synthesis of steroids and cell membranes). Since HMG-CoA reductase inhibitors decrease cholesterol synthesis and possibly the synthesis of other biologically active substances derived from cholesterol, they may cause fetal harm when administered to pregnant women. Therefore, HMG-CoA reductase inhibitors are contraindicated during pregnancy and in nursing mothers. **Pravastatin should be administered to women of childbearing age only when such patients are highly unlikely to conceive and have been informed of the potential hazards.** If the patient becomes pregnant while taking this class of drug, therapy should be discontinued and the patient apprised of the potential hazard to the fetus.

### WARNINGS

**Liver Enzymes:** HMG-CoA reductase inhibitors, like some other lipid-lowering therapies, have been associated with biochemical abnormalities of liver function. Increases of serum transaminase (ALT, AST) values to more than 3 times the upper limit of normal occurring on 2 or more (not necessarily sequential) occasions have been reported in 1.3% of patients treated with pravastatin in the U.S. over an average period of 18 months. These abnormalities were not associated with cholestasis and did not appear to be related to treatment duration. In those patients in whom these abnormalities were believed to be related to pravastatin and who were discontinued from therapy, the transaminase levels usually fell slowly to pretreatment levels. These biochemical findings are usually asymptomatic although worldwide experience indicates that anorexia, weakness, and/or abdominal pain may also be present in rare patients.

As with other lipid-lowering agents, liver function tests should be performed during therapy with pravastatin. Serum aminotransferases, including ALT (SGPT), should be monitored before treatment begins, every six weeks for the first three months, every eight weeks during the remainder of the first year, and periodically thereafter (e.g., at about six-month intervals). Special attention should be given to patients who develop increased transaminase levels. Liver function tests should be repeated to confirm an elevation and subsequently monitored at more frequent intervals. If increases in AST and ALT equal or exceed three times the upper limit of normal and persist, then therapy should be discontinued. Persistence of significant aminotransferase elevations following discontinuation of therapy may warrant consideration of liver biopsy.

Active liver disease or unexplained transaminase elevations are contraindications to the use of pravastatin (see CONTRAINDICATIONS). Caution should be exercised when pravastatin is administered to patients with a history of liver disease or heavy alcohol ingestion (see CLINICAL PHARMACOLOGY: Pharmacokinetics/Metabolism). Such patients should be closely monitored, started at the lower end of the recommended dosage range, and titrated to the desired therapeutic effect.

**Skeletal Muscle: Rhabdomyolysis with renal dysfunction secondary to myoglobinuria has been reported with pravastatin and other drugs in this class.** Uncomplicated myalgia has also been reported in pravastatin-treated patients (see ADVERSE REACTIONS). Myopathy, defined as muscle aching or muscle weakness in conjunction with increases in creatine phosphokinase (CPK) values to greater than 10 times the upper limit of normal was reported to be possibly due to pravastatin in only one patient in clinical trials (<0.1%). Myopathy should be considered in any patient with diffuse myalgias, muscle tenderness or weakness, and/or marked elevation of CPK. Patients should be advised to report promptly unexplained muscle pain, tenderness or weakness, particularly if accompanied by malaise or fever. **Pravastatin therapy should be discontinued if markedly elevated CPK levels occur or myopathy is diagnosed or suspected. Pravastatin therapy should also be temporarily withheld in any patient experiencing an acute or serious condition predisposing to the development of renal failure secondary to rhabdomyolysis, e.g., sepsis; hypotension; major surgery; trauma; severe metabolic, endocrine, or electrolyte disorders; or uncontrolled epilepsy.**

The risk of myopathy during treatment with lovastatin is increased if therapy with either cyclosporine, gemfibrozil, erythromycin, or niacin is administered concurrently. There is no experience with the use of pravastatin together with cyclosporine. Myopathy has not been observed in clinical trials involving small numbers of patients who were treated with pravastatin together with niacin. One trial of limited size involving combined therapy with pravastatin and gemfibrozil showed a trend toward more frequent CPK elevations and patient withdrawals due to musculoskeletal symptoms in the group receiving combined treatment as compared with the groups receiving placebo, gemfibrozil, or pravastatin monotherapy. Myopathy was not reported in this trial (see PRECAUTIONS: Drug Interactions). One patient developed myopathy when clofibrate was added to a previously well tolerated regimen of pravastatin; the myopathy resolved when clofibrate therapy was stopped and pravastatin treatment continued. **The use of fibrates alone may occasionally be associated with myopathy. The combined use of pravastatin and fibrates should generally be avoided.**

### PRECAUTIONS

**General:** Pravastatin may elevate creatine phosphokinase and transaminase levels (see ADVERSE REACTIONS). This should be considered in the differential diagnosis of chest pain in a patient on therapy with pravastatin.

**Homozygous Familial Hypercholesterolemia.** Pravastatin has not been evaluated in patients with rare homozygous familial hypercholesterolemia. In this group of patients, it has been reported that HMG-CoA reductase inhibitors are less effective because the patients lack functional LDL receptors.

**Renal Insufficiency:** A single 20 mg oral dose of pravastatin was administered to 24 patients with varying degrees of renal impairment (as determined by creatinine clearance). No effect was observed on the pharmacokinetics of pravastatin or its 3 $\alpha$ -hydroxy isomeric metabolite (SO 31,906). A small increase was seen in mean AUC values and half-life (t<sub>1/2</sub>) for the inactive enzymatic ring hydroxylation metabolite (SO 31,945). Given this small sample size, the dosage administered, and the degree of individual variability, patients with renal impairment who are receiving pravastatin should be closely monitored.

**Information for Patients:** Patients should be advised to report promptly unexplained muscle pain, tenderness or weakness, particularly if accompanied by malaise or fever.

**Drug Interactions:** Immunosuppressive Drugs, Gemfibrozil, Niacin (Nicotinic Acid), Erythromycin: See WARNINGS: Skeletal Muscle.

**Antipyrine:** Clearance by the cytochrome P450 system was unaltered by concomitant administration of pravastatin. Since pravastatin does not appear to induce hepatic drug-metabolizing enzymes, it is not expected that any significant interaction of pravastatin with other drugs (e.g., phenytoin, quinidine) metabolized by the cytochrome P450 system will occur.

**Cholestyramine/Colestipol:** Concomitant administration resulted in an approximately 40 to 50% decrease in the mean AUC of pravastatin. However, when pravastatin was administered 1 hour before or 4 hours after cholestyramine or 1 hour before colestipol and a standard meal, there was no clinically significant decrease in bioavailability or therapeutic effect. (See DOSAGE AND ADMINISTRATION: Concomitant Therapy.)

**Warfarin:** In a study involving 10 healthy male subjects given pravastatin and warfarin concomitantly for 6 days, bioavailability parameters at steady state for pravastatin (parent compound) were not altered. Pravastatin did not alter the plasma protein-binding of warfarin. Concomitant dosing did increase the AUC and C<sub>max</sub> of warfarin but did not produce any changes in its anticoagulant action (i.e., no increase was seen in mean prothrombin time after 6 days of concomitant therapy). However, bleeding and extreme prolongation of prothrombin time has been reported with another drug in this class. Patients receiving warfarin-type anticoagulants should have their prothrombin times closely monitored when pravastatin is initiated or the dosage of pravastatin is changed.

**Cimetidine:** The AUC<sub>0-12h</sub> for pravastatin when given with cimetidine was not significantly different from the AUC for pravastatin when given alone. A significant difference was observed between the AUC's for pravastatin when given with cimetidine compared to when administered with antacid.

**Digoxin:** In a crossover trial involving 18 healthy male subjects given pravastatin and digoxin concurrently for 9 days, the bioavailability parameters of digoxin were not affected. The AUC of pravastatin tended to increase, but the overall bioavailability of pravastatin plus its metabolites SO 31,906 and SO 31,945 was not altered.

**Gemfibrozil:** In a crossover study in 20 healthy male volunteers given concomitant single doses of pravastatin and gemfibrozil, there was a significant decrease in urinary excretion and protein binding of pravastatin. In addition, there was a significant increase in AUC, C<sub>max</sub>, and T<sub>max</sub> for the pravastatin metabolite SO 31,906. Combination therapy with pravastatin and gemfibrozil is generally not recommended.

In interaction studies with antiacids, [1 hour prior to PRAVACHOL (pravastatin sodium)], cimetidine, nicotinic acid, or probucol, no statistically significant differences in bioavailability were seen when PRAVACHOL was administered.

**Other Drugs:** During clinical trials, no noticeable drug interactions were reported when PRAVACHOL was added to diuretics, antihypertensives, digitalis, converting-enzyme inhibitors, calcium channel blockers, beta-blockers, or nitroglycerin.

**Endocrine Function:** HMG-CoA reductase inhibitors interfere with cholesterol synthesis and lower circulating cholesterol levels and, as such, might theoretically blunt adrenal or gonadal steroid hormone production. Results of clinical trials with pravastatin in males and post-menopausal females were inconsistent with regard to possible effects of the drug on basal steroid hormone levels. In a study of 21 males, the mean testosterone response to human chorionic gonadotropin was significantly reduced (p<0.004) after 16 weeks of treatment with 40 mg of pravastatin. However, the percentage of patients showing a  $\geq$ 50% rise in plasma testosterone after human chorionic gonadotropin stimulation did not change significantly after therapy in these patients. The effects of HMG-CoA reductase inhibitors on spermatogenesis and fertility have not been studied in adequate numbers of patients. The effects, if any, of pravastatin on the pituitary-gonadal axis in pre-menopausal females are unknown. Patients treated with pravastatin who display clinical evidence of endocrine dysfunction should be evaluated appropriately. Caution should also be exercised if an HMG-CoA reductase inhibitor or other agent used to lower cholesterol levels is administered to patients also receiving other drugs (e.g., ketoconazole, spironolactone, cimetidine) that may diminish the levels or activity of steroid hormones.

**CNS Toxicity:** CNS vascular lesions, characterized by perivascular hemorrhage and edema and mononuclear cell

infiltration of perivascular spaces, were seen in dogs treated with pravastatin at a dose of 25 mg/kg/day, a dose that produced a plasma drug level about 50 times higher than the mean drug level in humans taking 40 mg/day. Similar CNS vascular lesions have been observed with several other drugs in this class.

A chemically similar drug in this class produced optic nerve degeneration (Wallerian degeneration of retinogeniculate fibers) in clinically normal dogs in a dose-dependent fashion starting at 60 mg/kg/day, a dose that produced mean plasma drug levels about 30 times higher than the mean drug level in humans taking the highest recommended dose (as measured by total enzyme inhibitory activity). This same drug also produced vestibulocochlear (Wallerian-like degeneration and retinal ganglion cell chromatolysis) in dogs treated for 14 weeks at 180 mg/kg/day, a dose which resulted in a mean plasma drug level similar to that seen with the 60 mg/kg dose.

**Carcinogenesis, Mutagenesis, Impairment of Fertility:** In a 2-year study in rats fed pravastatin at doses of 10, 30, or 100 mg/kg body weight, there was an increased incidence of hepatocellular carcinomas in males at the highest dose (p<0.01). Although rats were given up to 125 times the human dose (HD) on a mg/kg body weight basis, their serum drug levels were only 6 to 10 times higher than those measured in humans given 40 mg pravastatin as measured by AUC.

The oral administration of 10, 30, or 100 mg/kg (producing plasma drug levels approximately 0.5 to 5.0 times human drug levels at 40 mg) of pravastatin to mice for 22 months resulted in a statistically significant increase in the incidence of malignant lymphomas in treated females when all treatment groups were pooled and compared to controls (p<0.05). The incidence was not dose-related and male mice were not affected.

A chemically similar drug in this class was administered to mice for 72 weeks at 25, 100, and 400 mg/kg body weight, which resulted in mean serum drug levels approximately 3, 15, and 33 times higher than the mean human serum drug concentration (as total inhibitory activity) after a 40 mg oral dose. Liver carcinomas were significantly increased in high-dose females and mid- and high-dose males, with a maximum incidence of 90 percent in males. The incidence of adenomas of the liver was significantly increased in mid- and high-dose females. Drug treatment also significantly increased the incidence of lung adenomas in mid- and high-dose males and females. Adenomas of the eye Harderian gland (a gland of the eye of rodents) were significantly higher in high-dose mice than in controls.

No evidence of mutagenicity was observed *in vitro*, with or without rat-liver metabolic activation, in the following studies: microbial mutagen tests, using mutant strains of *Salmonella typhimurium* or *Escherichia coli*, a forward mutation assay in L5178Y TK + / - mouse lymphoma cells, a chromosomal aberration test in hamster cells, and a gene conversion assay using *Saccharomyces cerevisiae*. In addition, there was no evidence of mutagenicity in either a dominant lethal test in mice or a micronucleus test in mice.

In a study in rats, with daily doses up to 500 mg/kg, pravastatin did not produce any adverse effects on fertility or general reproductive performance. However, in a study with another HMG-CoA reductase inhibitor, there was decreased fertility in male rats treated for 34 weeks at 25 mg/kg body weight, although this effect was not observed in a subsequent fertility study when this same dose was administered for 11 weeks (the entire cycle of spermatogenesis, including epididymal maturation). In rats treated with this same reductase inhibitor at 180 mg/kg/day, seminiferous tubule degeneration (necrosis and loss of spermatogenic epithelium) was observed. Although not seen with pravastatin, two similar drugs in this class caused drug-related testicular atrophy, decreased spermatogenesis, spermatocytic degeneration, and giant cell formation in dogs. The clinical significance of these findings is unclear.

**Pregnancy: Pregnancy Category X:** See CONTRAINDICATIONS.

Safety in pregnant women has not been established. Pravastatin was not teratogenic in rats at doses up to 1000 mg/kg daily or in rabbits at doses of up to 50 mg/kg/day. These doses resulted in 20x (rabbit) or 240x (rat) the human exposure based on surface area (mg/meter<sup>2</sup>). However, in studies with another HMG-CoA reductase inhibitor, skeletal malformations were observed in rats and mice. PRAVACHOL (pravastatin sodium) should be administered to women of child-bearing potential only when such patients are highly unlikely to conceive and have been informed of the potential hazards. If the woman becomes pregnant while taking PRAVACHOL, it should be discontinued and the patient advised again as to the potential hazards to the fetus.

**Nursing Mothers:** A small amount of pravastatin is excreted in human breast milk. Because of the potential for serious adverse reactions in nursing infants, women taking PRAVACHOL should not nurse (see CONTRAINDICATIONS).

**Pediatric Use:** Safety and effectiveness in individuals less than 18 years old have not been established. Hence, treatment in patients less than 18 years old is not recommended at this time. (See also PRECAUTIONS: General.)

### ADVERSE REACTIONS

Pravastatin is generally well tolerated; adverse reactions have usually been mild and transient. In 4-month long placebo-controlled trials, 1.7% of pravastatin-treated patients and 1.2% of placebo-treated patients were discontinued from treatment because of adverse experiences attributed to study drug therapy, this difference was not statistically significant. In long-term studies, the most common reasons for discontinuation were asymptomatic serum transaminase increases and mild, non-specific gastrointestinal complaints. During clinical trials the overall incidence of adverse events in the elderly was not different from the incidence observed in younger patients.

**Adverse Clinical Events:** All adverse clinical events (regardless of attribution) reported in more than 2% of pravastatin-treated patients in the placebo-controlled trials are identified in the table below; also shown are the percentages of patients in whom these medical events were believed to be related or possibly related to the drug

Body System/Event	All Events %		Events Attributed to Study Drug %	
	Pravastatin (N = 900)	Placebo (N = 411)	Pravastatin (N = 900)	Placebo (N = 411)
Cardiovascular				
Cardiac Chest Pain	4.0	3.4	0.1	0.0
Dermatologic				
Rash	4.0*	1.1	1.3	0.9
Gastrointestinal				
Nausea/Vomiting	7.3	7.1	2.9	3.4
Diarrhea	6.2	5.6	2.0	1.9
Abdominal Pain	6.2	6.9	2.0	3.9
Constipation	4.0	7.1	2.4	5.1
Flatulence	3.3	3.6	2.7	3.4
Heartburn	2.9	1.9	2.0	0.7
General				
Fatigue	3.8	3.4	1.9	1.0
Chest Pain	3.7	1.9	0.3	0.2
Influenza	2.4*	0.7	0.0	0.0
Musculoskeletal				
Localized Pain	10.0	9.0	1.4	1.5
Myalgia	2.7	0.0	0.6	0.0
Nervous System				
Headache	6.2	3.9	1.7*	0.2
Dizziness	3.3	3.2	1.0	0.5
Renal/Genitourinary				
Urinary Abnormality	2.4	2.9	0.7	1.2
Respiratory				
Common Cold	7.0	6.3	0.0	0.0
Rhinitis	4.0	4.1	0.1	0.0
Cough	2.6	1.7	0.1	0.0

\*Statistically significantly different from placebo.

The following effects have been reported with drugs in this class:

**Skeletal myopathy, rhabdomyolysis.**

**Neurological dysfunction** of certain cranial nerves (including alteration of taste, impairment of extra-ocular movement, focal paresis), tremor, vertigo, memory loss, paresthesia, peripheral neuropathy, peripheral nerve palsy.

**Hypersensitivity Reactions.** An apparent hypersensitivity syndrome has been reported rarely which has included one or more of the following features: anaphylaxis, angioedema, lupus erythematosus-like syndrome, polymyalgia rheumatica, vasculitis, purpura, thrombocytopenia, leukopenia, hemolytic anemia, positive ANA, ESR increase, arthritis, arthralgia, urticaria, asthenia, photosensitivity, fever, chills, flushing, malaise, dyspnea, toxic epidermal necrolysis, erythema multiforme, including Stevens-Johnson syndrome.

**Gastrointestinal:** pancreatitis, hepatitis, including chronic active hepatitis, cholestatic jaundice, fatty change in liver, and, rarely, cirrhosis, fulminant hepatic necrosis, and hepatoma, anorexia, vomiting.

**Reproductive:** gynecomastia, loss of libido, erectile dysfunction.

**Eye:** progression of cataracts (lens opacities), ophthalmoplegia.

**Laboratory Test Abnormalities:** Increases in serum transaminase (ALT, AST) values and CPK have been observed (see WARNINGS).

Transient, asymptomatic eosinophilia has been reported. Eosinophil counts usually returned to normal despite continued therapy. Anemia, thrombocytopenia, and leukopenia have been reported with other HMG-CoA reductase inhibitors.

**Concomitant Therapy:** Pravastatin has been administered concurrently with cholestyramine, colestipol, nicotinic acid, probucol and gemfibrozil. Preliminary data suggest that the addition of either probucol or gemfibrozil to therapy with lovastatin or pravastatin is not associated with greater reduction in LDL cholesterol than that achieved with lovastatin or pravastatin alone. No adverse reactions unique to the combination or in addition to those previously reported for each drug alone have been reported. Myopathy and rhabdomyolysis (with or without acute renal failure) have been reported when another HMG-CoA reductase inhibitor was used in combination with immunosuppressive drugs, gemfibrozil, erythromycin, or lipid-lowering doses of nicotinic acid. Concomitant therapy with HMG-CoA reductase inhibitors and these agents is generally not recommended. (See WARNINGS: Skeletal Muscle and PRECAUTIONS: Drug Interactions.)

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# JOURNAL

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## SCIENTIFIC ARTICLES

- An Assessment Of Obstetric Services** 143  
**In Mississippi**

*D. Leigh Copeland, BA; William H. Replogle, PhD;  
G. Rodney Meeks, MD; John C. Morrison, MD;  
Kenneth P. Pittman, MD; and Stephen M. Crane, MD*

- Slipped Capital Femoral Epiphysis, A Problem** 147  
**Of Diagnosis**

*Ronald J. Kendig, MD; Larry Field, MD; and  
Luther C. Fisher, III, MD*

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## EDITORIALS

- The WALT Principle** 154

*Don Q. Mitchell, MD*

- Same Song: Last Verse** 155

*Joseph E. Johnston, MD, Associate Editor*

## DEPARTMENTS

- Comments** 157  
**Medical Organization** 161  
**The University of Mississippi Medical Center** 167  
**Personals** 169  
**Information for Authors** 173  
**Placement Service** 175  
**Classified** 177

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## Medicare pay too low

Boston - Medicare doesn't pay physicians enough, say a new analysis. The Harvard study says care for the elderly will suffer unless private insurers continue to pay high rates to subsidize their care. The chief author is William C. Hsiao, PhD, creator of Medicare's RBRVS. If all insurers paid Medicare rates, the study says, pediatricians would earn \$35,000 a year, family physicians \$40,000 and general internists \$44,000. At the other end of the scale, orthopedic surgeons would earn \$174,000 and thoracic surgeons \$241,000.

\*\*\*

## Vaccine program proposed

Washington- Children's advocates applaud a \$1.1 billion administration plan to provide vaccinations for all children at government expense. Free vaccine would go to private physicians and public clinics in states participating in a national immunization-tracking network. Elsewhere, the free vaccine would go to public providers. Leading vaccine makers, who have tried to dissuade the government from making itself the sole purchaser of childhood vaccines, say the plan actually might discourage new vaccine development.

\*\*\*

## Award recognizes new route to CME

Chicago - To encourage physicians to become more self-directed in their continuing medical education, the AMA has introduced a new version of its Physician's Recognition Award.

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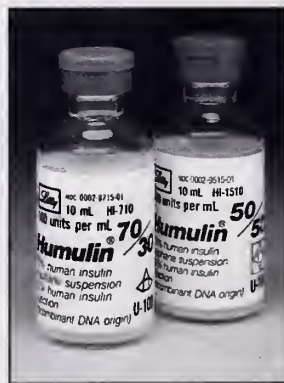
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# An Assessment Of Obstetric Services In Mississippi

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**T**he availability of obstetric care is declining in this nation. This shortage is due primarily to the increasing number of physicians who no longer offer obstetrics as part of their routine practices. Family physicians and general practitioners seem to account for a disproportionate reduction in obstetric services as determined by studies from other states.<sup>1-8</sup> Approximately 28% of active members of the American Academy of Family Physicians (AAFP) reported that they offered obstetric care in 1988.<sup>9</sup> This differs from a similar AAFP study conducted in 1980 in which over 36% of active members provided routine obstetric care.<sup>10</sup>

Historically, family physicians and general practitioners have provided rural obstetric care and are twice as likely to have routine obstetric privileges as their urban counterparts.<sup>9</sup> Indeed, a recent survey

Seven hundred and six (80.6% response rate) obstetricians, family physicians, and general practitioners responded to a survey designed to elicit information regarding their obstetric practice. Results of the study were compared to a similar survey conducted in 1985. The proportion of obstetricians offering obstetric care has remained relatively constant since 1985. Among family physicians and general practitioners, however, there was a significant decrease in the proportion who practice obstetrics ( $p < .01$ ), and a significant increase in the proportion who have discontinued obstetric practice in the last five years ( $p < .01$ ) and who plan to discontinue obstetric care in the next five years ( $p < .05$ ). Consistent with the 1985 data, cost of malpractice insurance, threat of litigation, and time demand were the three most frequently reasons for discontinuing obstetric care. Without changes in the current system, the provision of obstetric care in rural areas will continue its current dramatic decline.

of Family Practice Residency graduates in Alabama reported that no graduates provided private obstetric services in municipalities larger than 25,000.<sup>8</sup>

The decline in this provider pool has greatly impacted the availability of obstetric services in rural areas. With few obstetrician gynecologists es-

establishing practices in these areas of decline, and fewer family practice graduates including obstetrics in their practices, this void is unlikely to be filled.

Mississippi is a largely rural state with only seven of its 82 counties classified as Standard Metropolitan Statistical Areas. The remaining 75 counties are classified as rural. This rural environment combined with the steady decline in obstetric care could have a major impact on the quality of health care received by pregnant patients. In 1985 Wiygul et al reported that 35% of family physicians and 23% of general practitioners in Mississippi delivered obstetric care. However, 23% of family physicians and 30% of general practitioners who were practicing obstetrics indicated plans to discontinue this service within five years.<sup>1</sup>

The purpose of this study is to ascertain the availability of obstetric care in Mississippi based on independent surveys of practitioners and hospitals offering perinatal services.

## Method

A roster of all family physicians, general practitioners, and obstetrician-gynecologists registered in 1991 to practice medicine in Mississippi was obtained from the Mississippi State Medical Association. A single page questionnaire, requiring less than 5 minutes to complete, was distributed to the 901 physicians identified. Twelve days after the original mailing, a second, identical questionnaire was sent to non-respondents.

The questionnaire was designed to determine whether physicians were currently providing obstetric care and if so,

whether they planned to discontinue this service within the next 5 years. For physicians who indicated they were either not performing deliveries or planned to discontinue, a list of possible factors determining their decision was provided. The data obtained were then compared to a similar survey conducted in 1985.<sup>1</sup>

Twenty-two questionnaires were returned as non deliverable. Of the remaining 879 questionnaires, 706 (80.3%) were completed. The response rate by specialty group was 174 (86.5%), 459 (80.3%), and 73 (68.2%) for obstetricians, family physicians, and general practitioners, respectively. The mean age of respondents was  $49.0 \pm 12.9$  years (mean + SD).

In 1991 the Mississippi State Department of Health independently queried administrators of Mississippi hospitals providing perinatal service to elicit information on the availability of obstetric care at their institution. To be defined as a physician who delivers obstetric care, obstetricians had to

perform at least 3 deliveries per month while family physicians as well as general practitioners had to perform at least two deliveries per month in those institutions. One hundred percent of the hospitals responded to the survey.

A two tailed z-approximation was used to compare proportions. The text presents data separately for family physicians and general practitioners. All inferential statistics and associated probability levels, however, are based on the combination of these two groups as presented in Table 1. An alpha of .05 was used to determine significance.

## Results

The proportion of physicians practicing obstetrics has decreased since Wiygul's<sup>1</sup> report of 1985. (Table 1) Among obstetricians there was not a significant decline in those offering obstetric services. There was, however, a significant reduction in the proportion of family physicians and general practitioners who practice ob-

Table 1 — Summary and Comparison of Physicians Surveys

	Obstetricians	Family Physicians & General Practitioners
% offering obstetric care		
1985 <sup>1</sup>	95.0	31.5
1991	90.7	8.5**
% discontinuing obstetric care in past 5 years		
1985	5.0	33.8
1991	4.3	72.5**
% expecting to discontinue obstetric care in next 5 years		
1985	23.0	25.5
1991	28.7	41.5*
* p < .05		
** p < .01		



stetrics ( $z=8.9$ ,  $p<.01$ ). In 1985, 35% of family physicians and 23% of general practitioners included obstetric care in their practices. Results indicate that now only 8.8% of family physicians and 7.0% of general practitioners practice obstetrics. Of the physicians who were delivering obstetrics in 1985, 57% were either family physicians or general practitioners while 42% were obstetricians. This ratio had significantly changed in 1991 when only 22% of physicians offering obstetric care were family physicians or general practitioners and 78% were obstetricians ( $z=7.2$ ,  $p<.01$ ).

The proportion of family physicians and general practitioners who have discontinued obstetrics in the past five years has significantly increased since 1985. ( $z=11.6$ ,  $p<.01$ ) Results from 1985 indicated 31% of family physicians and 41% of general practitioners had discontinued practicing obstetrics in the past 5 years. However, the current results indicate 66% of family physicians and 72% of general practitioners discontinued such services in the past 5 years. Interestingly, Wiygul's survey reported that 23% and 30% of family physicians and general practitioners, respectively, anticipated discontinuing their obstetric practices in the next 5 years. Our data show that the actual decline is more than twice the rate projected in 1985.

Among physicians who currently practice obstetrics, 28.7% of the obstetricians plan to discontinue in the next five years, which represents no change since 1985. There has been a significant increase in the proportion of family physi-

cians and general practitioners who plan to discontinue obstetric services ( $z=2.07$ ,  $p<.05$ ). Current data indicate 41.7% of family physicians and 40% of general practitioners plan to discontinue obstetrics within the next five years as compared to 23% and 30% in 1985.

The most frequently cited factors determining the decision to no longer offer obstetric care among physicians who had either discontinued this service over the past 5 years or who planned to discontinue in the next 5 years were cost of malpractice insurance, threat of litigation, and time demand. (Table 2) These mirror the most frequently cited reasons reported in 1985.<sup>1</sup>

The survey of practitioners identified 158 obstetricians and 45 family physicians/general practitioners delivering obstetric care. The survey of hospitals providing perinatal service identified 158 obstetricians and 41 family physicians/general practitioners providing obstetric care in 1991. Concordance of the two independent surveys indicate high reliability of study findings.

## Discussion

A decline in physicians who provide obstetric care is occur-

ring nationally. This decline may pose a serious threat to the availability of obstetric care, now and in the future. Our data indicates a more dramatic decline in availability of obstetric services than predicted by Wiygul et al. The projection made by Wiygul et al in 1985 for the next five years was a reduction of 108 physicians delivering obstetrics.<sup>1</sup> The obstetric provider pool was estimated by Wiygul to be from 400-470 physicians in 1985. Current data indicates a reduction to 203 physicians, approximately double the expected decline. Thus our data indicates a more dramatic reduction than projected in obstetric manpower.

Additionally, the pool of obstetric care providers is no longer equally distributed among family physicians, general practitioners, and obstetricians as it is now one of mostly obstetricians. Indeed, the percentage of family physicians and general practitioners who have discontinued obstetrics has been dramatic and disproportionate. Most importantly this distribution directly effects the obstetric care force in rural areas. Thus, rural states such as Mississippi may have more difficulty providing obstetric services.

Table 2 — Reasons Cited For Discontinuing Obstetric Care

	Total %	Obstetricians %	Family Physicians & General Practitioners %
Cost of malpractice insurance	53	44	64
Threat of litigation	43	41	46
Time demand	34	28	41
Reimbursement not comensurate with cost	24	24	25
Lack of cross coverage	14	9	21
Volume too low	7	2	11



According to the AAFP, there is a similar flight from obstetrics nationwide.<sup>9</sup> Family physicians are no longer choosing to provide obstetric care as they have in the past. When asked what factors influenced their decision to leave obstetrics, respondents listed cost of malpractice insurance, threat of litigation, and time demand. For some physicians whose obstetric practice is one of low volume, the high cost of malpractice insurance for such a limited number of patient encounters often precludes the delivery of obstetric care. Others may find the constant demand on their time to be confining. Furthermore, as more physicians choosing to exclude obstetrics from their practice, fewer partners are available to assist with the time burden.

Considering these major factors resulting in the abandonment of obstetric care, what are possible solutions? The Alabama legislature has approved a Family Practice Rural Health Board which, among other things, will subsidize family practice obstetric fellowship positions and malpractice insurance premiums. Fellowship recipients must agree to rural practices.<sup>8</sup> Kentucky has created a regional primary care obstetric unit staffed by family physicians to provide obstetric care in an area with a large proportion of indigent patients. Since the creation of this program, the number of patients who deliver without prenatal care has decreased from 3.0% to .07%.<sup>4</sup>

These programs offer excellent alternatives for combating the factors that deter physicians from providing ob-

stetric care. Other innovative programs must be initiated to address the issue of providing obstetric care. Provision of this element of health care must be available in the local area. Ingenuity must be the guide for policy makers and health care planners. Without changes in the current system, the provision of obstetric care in rural areas will continue its current dramatic decline. □

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## COMMENTS or QUERIES....

The Editors of *Journal MSMA* invite you to comment on any material that appears in or is absent from the publication.

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# Slipped Capital Femoral Epiphysis, A Problem of Diagnosis

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**D**elay in diagnosis and treatment of slipped capital femoral epiphysis is a common problem in Mississippi. Our recent review of 48 slipped capital femoral epiphysis revealed that the average duration of symptoms before diagnosis was 10 months. In 31% of these cases the physician who initially evaluated the patient did not make the correct diagnosis resulting in significant delay and morbidity. This resulted in a high percent of very severe slips in this study. This article will review the etiology, epidemiology, natural history, presentation, physical examination, radiologic evaluation, treatment, and complications of slipped capital femoral epiphysis.

## Natural History

A slipped capital femoral epiphysis is a displacement of the capital femoral epiphysis through the growth plate relative to the femoral neck (fig. 1A & B). Most often this displacement occurs slowly and relentlessly over time (chronic-slip); however, marked displacement may occur suddenly and unexpectedly (acute-slip). The slippage of the epiphysis is usually posterior and medial to the femoral neck. In the acute slip pain is severe and the displacement is significant. The patient seeks medical attention



*Fig. 1 A & B — This is a mild left slipped capital femoral epiphysis that is most evident on the lateral view. Findings include a widened physis on the lateral image, decreased epiphyseal height on the AP image, and a line through the center of the neck that does not fall through the center of the head on the lateral view. Slips detected at this stage have a good prognosis.*



promptly and the physician can usually make the diagnosis easily. In the chronic slip symptoms are often mild and the slip minimally affects activity levels. The physician can easily miss the diagnosis if he or she is not alert to this problem. Often the physician passes off the initial presentation cursorily as a pulled muscle. Sometimes symptoms initially are totally absent (silent-slip). Bilateral slips may occur as much as 60% of the time.<sup>4,5</sup> As the deformity progresses, the range of motion of the hip becomes restricted with loss of internal rotation, flexion, and abduction. Without treatment, deformity may become severe before eventually stabilizing after growth plate closure. Severe deformity likely leads to premature osteoarthritis.<sup>6,12</sup> Mild deformity may also cause osteoarthritis, but usually later in life.<sup>13,14</sup> Severe deformity is also associated with catastrophic complications such as chondrolysis and avascular necrosis. These complications often cause total loss of hip function in the adolescent via severe arthritis sometimes requiring hip fusion or replacement.

### **Epidemiology**

Slipped capital femoral epiphysis usually occurs early in the adolescent growth spurt (~12-15 males, ~10-13 females). The incidence of slipped capital femoral epiphysis is related to race, sex, and geography. Blacks, males, and inhabitants of the eastern U.S.A. have higher rates than their counterparts. For example, the black male rate in Connecticut is 7.79/100,000 compared to an incidence of 0.71/100,000 in New Mexico.<sup>8</sup>

### **Etiology**

The etiology of slipped capital femoral epiphysis is not defi-

nitely known; however, there are several factors that play a role. The clearest association is between mechanical factors and the slippage. Patients are large for their age, sexual maturity, and height. J. Kelsey et al in 1972 showed that about 50 percent of the patients in their series had weights above the 95th percentile for their age and height.<sup>7</sup> Additionally the femur is more retroverted (excessive external-twist) than normal in these patients.<sup>3</sup> These factors put unusual stress on the growth plate and movement through the plate slowly occurs.

Mechanical factors are not the only problem. There is probably some abnormality that weakens the growth plate itself. Endocrinologic factors such as growth hormone, testosterone, and thyroid-hormone may play a role though the literature has not clearly defined their role. Slipped capital femoral epiphysis is a well-known complication of various endocrinopathies such as hypothyroidism, hypogonadism, pituitary dysfunction and its treatment, and renal osteodystrophy. The physician may occasionally initially recognize these endocrinologic problems because of the slip. The physician should consider these problems in patients presenting outside the typical age group or with other atypia.

Immunologic factors and associated synovitis may also contribute to growth plate weakness.<sup>10,11</sup> Hereditary factors are difficult to differentiate from environmental influences but in one study 5% of the patients' parents also had slipped capital femoral epiphysis.<sup>17</sup>

### **Presentation**

The chronic slipped capital femoral epiphysis may present subtly. Patients will initially have hip

or knee pain and perhaps a mild limp that they associate with activity. Medial knee pain is common as a sole presenting symptom because it is referred from the hip via the obturator nerve. Referred hip pain to the knee is one of the most common reasons for delay in diagnosis of slipped capital femoral epiphysis. As the slip becomes more severe, the patients develop a worsening limp and progressive out toeing.

On physical-exam the hip has diminished range of motion particularly internal rotation, abduction, and flexion. A near pathognomonic sign is a hip that externally rotates as the physician flexes it, particularly in the obese adolescent (fig.2).

X-ray evaluation is confirmation of the suspected diagnosis but the findings may be subtle. The proper x-rays to obtain are a supine AP pelvis and a frog leg lateral of each hip. The latter is the most sensitive to the mild slip because usually the epiphysis primarily moves posterior to the femoral neck. Normally a line drawn parallel to and through the center of the femoral neck should pass through the center of the epiphysis on both views. Be wary of comparing with the opposite hip since many cases are bilateral. Often the physis will appear widened and the epiphyseal height diminished.

Sometimes a hip will be symptomatic before x-ray findings occur (pre-slip). These patients are often clinically suspect because they are in the right age group and obese. They need careful consideration for possible treatment and the physician should refer them to an orthopaedic surgeon.

Patients in whom the physician has made the diagnosis need urgent referral for definitive treatment. They are prone to acute and sudden worsening of their defor-





**Fig. 2** — This patient demonstrates a characteristic physical sign of slipped capital femoral epiphysis. Her hip externally rotates as the examiner flexes the hip.



**Fig. 3** — This patient had a mild chronic slipped capital femoral epiphysis when first diagnosed by a physician four days prior to referral. This progressed acutely to a severe slip during this four day interval. This case demonstrates the urgency of referral necessary when the diagnosis is made or suspected.

mity with the mere step off a curb or the inadvertent twist of the leg (fig 3). Their physician should give them crutches (toe touch weight bearing), and/or place them at bed rest until they arrange for transportation and definitive treatment.

### Treatment

The goals of treatment are to prevent progression of the deformity. Osteotomies of the femoral neck and growth plate to restore normal anatomy generally have an excessive severe complication rate; thus, it is important to recognize

this problem early and prevent severe deformity.

The most common way to prevent progressive deformity today is to perform in situ fixation of the epiphysis with a single 7mm screw (fig. 4 A&B). The screw enters the anterior lateral femoral neck or metaphysis. We can usually do this percutaneously with a tiny incision, by use of intraoperative X-ray and cannulated bone screws. Acute unstable slipped epiphyses require greater fixation or a second screw. Some people treat slips with an open epiphysiodesis or a spica cast;<sup>9,16</sup> both are effective but more complex treatments. These methods lead to epiphyseal closure. This does not cause a significant limb length difference since these patients are close to maturity and this growth plate contributes only about 10% of limb length.

Most of the time, the residual deformity of the proximal femur does not cause a functional problem for the patient during adolescence. Occasionally, if the patient has a persistent severe restriction of motion and a limp, we can improve these problems with a subtrochanteric osteotomy. We usually delay this treatment several years after initial in situ fixation as sometimes range of motion and hip function will improve due to capsular and bone remodeling during this time.

### Complications

The most common complications are chondrolysis and avascular necrosis. The surgeon may or may not induce these iatrogenically. Chondrolysis is the most common. It is associated with severe slips, black females, femoral osteotomies, and inaccurate in situ fixation (the screw or pins left extended into the joint). More recent series with fewer severe slips using more accurate techniques of single screw fixation seem to have reduced but



**Fig 4 A&B.** — This case demonstrates the placement of a single screw percutaneously under intra-op X-ray in a severe chronic slipped capital femoral epiphysis.

not eliminated this complication.<sup>1,15</sup> We do not know the triggering mechanism for chondrolysis but there is some evidence immunologic factors might play a role.<sup>2</sup>

Chondrolysis presents with hip pain and stiffness that progressively worsens. These symptoms are usually more severe than in the typical chronic slipped capital femoral epiphysis. Radiologically the joint space narrows. The patients often develop a hip flexion/

adduction contracture. Sometimes chondrolysis spontaneously improves over 1-2 years, especially in patients with less severe deformity. More often the hip progressively worsens and becomes ankylosed eventually requiring fusion or hip replacement. Occasionally subtotal capsulectomy and contracture release is helpful in restoring some hip function. Treatment initially is supportive with crutches, anti-inflammatory drugs,

and physical therapy.

Avascular necrosis is the most devastating complication because it often leads to irreversible deformity and inevitable osteoarthritis due to joint incongruity. Avascular necrosis is associated with acute slips and with forceful attempts of manipulation of slips. Additionally, avascular necrosis is associated with femoral neck osteotomies, and perhaps placement of screws and pins in the anterior lateral portion of the epiphysis. Treatment initially is supportive with ambulatory aids and anti-inflammatories. Hip fusion and replacement are alternatives later, if the patient's symptoms warrant.

### Conclusions

1. Early recognition to prevent severe deformity is the most important controllable factor in reducing morbidity and complications from slipped capital femoral epiphysis. The long term natural history of slipped capital femoral epiphysis is not totally clear but severe deformity is associated with premature degenerative arthritis.

2. Suspect this condition in obese children between ages 10-15. Promptly and thoroughly evaluate any limp, hip, thigh or knee pain in this age group. Refer these patients urgently for definitive care.

3. Technologic advances in imaging and bone fixation have reduced complications and the difficulty of treatment. □

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*Dr. Kendig is an Assistant Professor, Dr. Field is a Resident and Dr. Fisher is an Associate Professor all in the Department of Orthopaedic Surgery, University Medical Center.*

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## The President's Page

DON Q. MITCHELL, MD

### The WALT Principle

**T**wo years ago at the AMA Annual Meeting, I heard a short talk that really caught my attention. It contained some friendly advice about being a doctor and the speaker used the acronym — WALT — to make his points.

**W - Walk Like A Doctor**

**A - Act Like A Doctor**

**L - Look Like A Doctor**

**T - Talk Like A Doctor**

I have thought about WALT's varied characteristics frequently over the past two years. These characteristics become particularly important as I begin my year of representing you as president of this association.

I realize that WALT is not just a single stereotype of a doctor, but rather a collage of what each of us brings to the profession.

**Walk like a doctor** - It is the easy stride of the confident outgoing doctor on rounds. It is quiet and introspective pacing to mull over a patient's condition.

**Act like a doctor** - It is both being compassionate and caring with a patient or when necessary being detached and objective in making a critical judgment. It is also being a respected, involved member of the community.

**Look like a doctor** - Our first mental image is usually the older, distinguished physician, but isn't it rather a combination of each of us with our respective differences?

**Talk Like A doctor** - It is talking knowledgeably about the profession and about health care issues. It is speaking out on the larger issues of society as well as those of the profession.

At this point, we must ask the following questions about talking like a doctor:

*(Continued on page 156)*



## Same Song: Last Verse

Ten years pass quickly when you're having fun. I have enjoyed writing editorials during this period of time, but I feel that younger and different views are needed to move forward. You have been a good audience and I have appreciated all the comments both pro and con given toward my editorials.

Speaking of the "audience", I almost entitled this one "Barking Up The Wrong Tree" for I sometimes feel that we should be writing for audiences other than just ourselves. I am reminded of Barry Goldwater's race for presidency many year ago. I was traveling all over the country on many boards and committees at the time, and every where I went the people I talked to all felt that he would surely be president.... well, you know the outcome of that. What I am saying is that every medical journal has some good editorials that we all agree with, but they are read for the most part by physicians that already believe the same as the authors, rather than being read by someone who can either make a

change as a result of reading the article or at least influence a change. The present proposed drastic changes in the health care delivery systems is no exception, as I think most of you reading this feel the same as I do. The problem is that we can do little to influence the government to see our side.

I visit with some 250 "Votes" each week just as most of you do. *If we can influence these votes to help us with the changes we want, then we can succeed. I promise to try to be a better, more informed, and more effective spokesman for organized medicine.... won't you?*

*The winds of change are constantly seeking to alter the face of medicine.... stronger now than ever before. May these winds serve as forces for renewal and improvement in our efforts to provide the very best care for our patients.*

*Thank God I am a physician.*

**Joseph E. Johnston, MD**  
Associate Editor

The editorial opinions expressed in this Journal are those of the indicated author. Editorial opinions are not expressions of the views, or official policies of The Mississippi State Medical Association. We encourage the membership to submit letters for publication regarding any opinion expressed or information contained in the Journal.

**President's Page**  
(Continued from page 154)

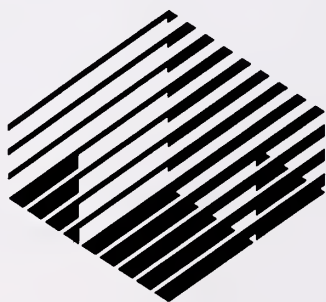
Is there one resonance? One accent? Do physicians speak with one voice?

As president of your association, I face a formidable task in representing such a vast spectrum of images. However, having grown up in the Mississippi Delta, having lived the past thirty years of my life married to the daughter of a small-town family practitioner, and having spent eighteen years of practice as a specialist in Jackson, I feel I am prepared to be your WALT.

I'll try to remember who I am and who I represent, and at all times walk, act, look and talk like what we all should be proud to be ... doctors.

Your colleague,

*WALT*



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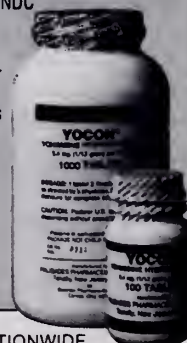
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**The *Journal* MSMA received a copy of the following letter:**

**Dear First Lady Clinton,**

The Federal Government is about to create a new world order for Health Care in the United States of America. It is certainly possible that the United States Government will create a socialist fiasco complete with central planners who rule by decree. Whoever controls the funds will control the American Health Care System. If physicians become de-facto salary employees of either the government or hospitals, all of the incentive will be stacked against service to individual patients.

From the physicians point of view, the core financial incentive issue should be payment for service that is based upon units of service provided to patients. The dollar value for these units of service will have to be negotiable between payers and providers. If there is going to be meaningful change of the health care system, there must be suspension of torts claims liability and suspension of federal anti-trust liability for both physicians and hospitals. A radical simplification of claims payment process is long overdue and has been certainly technologically feasible for several years. Insurance premiums must have a community basis rather than group

risk basis. We must have a system that pays for the work that is done and encourages workers to innovate. Patients will not have an advocate if physicians become employees of the government or hospitals; physicians will have to do what the employer requires of them. In our current system, the patient is the physician's employer on a case by case basis. That is the paramount advantage that patients have, and this must not be lost.

Sincerely yours,  
**Philip Saccoccia, Jr., MD**  
Chief of Staff  
Memorial Hospital  
at Gulfport □

### On Appreciating Patients

In late March, hospitals all over the country observed National Doctor's Appreciation Day by honoring their medical staffs with continental breakfasts, pinning carnations on their lab coats and snapping photos of their smiling visages for surreptitious publicity in hometown newspapers. Sure, hospital administrations appreciate their doctors. The reasons for this are obvious; most of them have to do with the physicians' ability to generate significant amounts of revenue for their hospital.

Patients show their appreciation to their personal physicians with relative frequency. Verbal expressions of thanks, friendly hugs, shared Clinton jokes, wa-

termelons in season, crocheted doo-hickeys, and stacks of fried peach pies.... these things, not money, keep me coming to the office every day. The desire to get rich never entered the picture. I didn't watch ten seasons of "Dallas" without learning something. Being rich only buys you more expensive forms of misery.

I have a deep-rooted desire to be needed and appreciated. Without benefit of statistical evidence as proof, I would venture to say that this is the real reason most doctors go into medicine in the first place.

But, do we doctors appreciate our patients as much as we should? No matter how idealistically we started out, by the end of the senior year of med school

patients have become the "enemy." We are trained in a militaristic fashion. The lowest ranking members receive their clinical education by performing the most menial tasks and putting in the longest hours. Excessive time required by a patient is perceived to take away precious minutes needed to prepare for written examinations. Admitting a patient while on night duty is known as "taking a hit." The more patients you get, the more sleep you lose. On work rounds the next morning you are not asked how many folks you treated last night, but rather "how bad did they hurt you?"

Do we appreciate patients enough? The truth is sometimes we don't even like some of our patients. When I look at my daily



appointment roster each morning there is always a name or two that pops up which elicits a groan of dread from the nurses and renders me momentarily weak and dizzy. But, when they come in (and they always do) we are as cordial and helpful as humanly possible. All in the line of duty.

Then there are times when I have a patient that downright makes me hate them. They don't necessarily have to be evil people to elicit that ranor. The manipulators, the habitual liars, and the chronically self-destructive types are particularly insufferable. I've learned through the years to be pretty good at not letting it show. This seems somewhat counter-productive, because they keep coming back. I suspect it is because nobody else even pretends to tolerate them. I once heard that if you've never hated your children you've never really been a parent. It is my belief that if a doctor has never felt utter animosity for a particular patient, it must mean the ink is still wet on his diploma.

Simply stated, doctors should appreciate their patients more than we do. Most of us would if we thought about it much.

I appreciate it when patients say "That's all right, I didn't mind waiting for you, Doc," when I'm running late, instead of snarling at me.

I appreciate it when patients tell me I look nice, even when I don't.

I appreciate it when patients share something very personal or touching with me and end by saying "I've never told that to anyone else before."

I appreciate patients who smell nice.

I appreciate my terminally ill patients. Dying people teach us the best lessons about living with grace and dignity.

I appreciate the vast diversity of humanity that passes through my doorway daily. I've never had even one boring day at work.

I appreciate the great stories both tragic and comic that people share with me everyday. Through my patients my human experience has been enriched beyond words.

I appreciate honest patients who tell me when they can't pay me. It saves us both a lot of grief.

I appreciate my hypochondriacs. They are responsible for paying my utility bills.

I appreciate the fact that there are people who have known me since I was a kid who actually are brave enough to come see me. I'm still awestruck when my elementary school principal comes to me for advice.

I appreciate my patient who is an engineer and world traveler who brings me something from

every country he visits, coffee from South America, copper bracelets from Kenya, and a XXL grass skirt and coconut bra from Hawaii. Since I can't get away much, I travel vicariously through him. It's great fun when he gets back from a trip.

I have even learned to appreciate it when people ask me medical questions while I'm grocery shopping or eating out. Many people don't quite know what to say to a doctor so asking for advice is very often simply a form of sincere flattery. Of course, this isn't really always the case, but it helps your blood pressure if you pretend. It took me a long time to learn this.

I appreciate the fact that my patients will never permit me to stop learning.

In a capsule, Physicians . . . appreciate your patients! Patients enrich our lives every day and enable us to make a good living in our hometown doing a most valuable and enjoyable work.

You don't have to pin a corsage on their lapels. Just once in a while say, "Thank you for being my patient."

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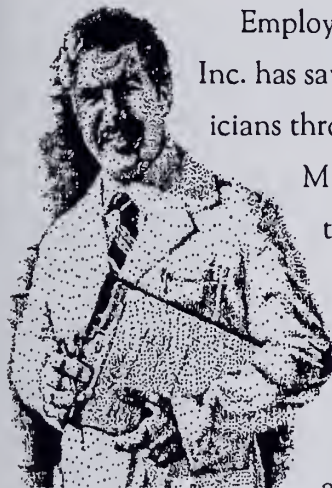
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## Mississippi Physicians Participate in National Coalition Against Family Violence

During the past two years, as part of its campaign against family violence, the American Medical Association has been recruiting members into a National Coalition of Physicians Against Family Violence. Membership is free of charge and open to interested physicians, alliance members, and professionals working in the field of public health and advocacy.

There are now approximately 4,000 members in the coalition, and all have received membership materials including the set of four AMA Diagnostic and Treatment Guidelines on Child Abuse and Neglect, Child Sexual Abuse, Elder Abuse and Neglect and Domestic Violence.

Sixteen Mississippi Physicians are currently members of the National Coalition. They are: **Cheryl L. Branche, MD**, Belzoni; **Rose Casano, MD**, Jackson; **Linda Chidester, MD**, Mantachie; **John J. Davis, Jr., MD**, Meridian; **Darlene Dotherow, MD**, Brandon; **Peter S. Kamp, MD**, Hattiesburg; **Leland R. Kendrick, MD**, Jackson; **Earl Mahaffey, MD**, Sebastopol; **William L. Marcy, MD**, Tupelo; **James R. Medlin, MD**, Ecrú; **Phillip T. Merideth, MD, JD**, Jackson; **W. A. Middleton, MD**, Winona; **Max L. Pharr, MD**, Jackson; **Craig Slater, MD**, Gulfport; **Erlinda Vidanes-Alcalen, MD**, Bay St.

Louis; and **Jonathan Wynstra, MD**, Biloxi.

If you would like to join the AMA National Coalition of Physicians Against Family Violence,

please complete the form below and send it to the Department of Mental Health, American Medical Association, 515 N. State Street, Chicago, Illinois 60610.

### ENROLLMENT FORM

Please enroll me in the AMA National Coalition of Physicians Against Family Violence

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#### Areas of interest within Family Violence

\_\_\_\_\_ Child Abuse \_\_\_\_\_ Sexual Abuse

\_\_\_\_\_ Domestic Violence \_\_\_\_\_ Elder Abuse

\_\_\_\_\_ Other

\_\_\_\_\_

## Dr. Lee Appointed to Risk Pool Association Board

Commissioner of Insurance George Dale has appointed Dr. John P. Lee of Forest for a three-year term to the board of directors of the Mississippi Comprehensive Health Insurance Risk Pool Association.

The association was created by the Mississippi Legislature in 1991 to provide health insurance coverage for those persons whose prior medical history makes them uninsurable. The Pool has a capacity for almost 2,000 state residents, and all health insurance companies licensed in the state are assessed to fund the program.

Dale said, "Dr. Lee is highly respected in the medical community, and I believe he will make a significant contribution to the association. Being a family practitioner, he is exposed to all aspects of medicine and will bring insight on how the program can best benefit the people who can participate in the program."

A former resident of Carthage, Dr. Lee completed his under graduate degree in chemistry and his MD degree from the University of Mississippi.

After completing internship at the U. S. Naval Hospital in San Diego, California, he served in the Navy from 1968-72 and completed a general surgery residency at University Medical

Center Jackson.

Dr. Lee has been practicing family medicine in Forest since 1973 where he has served as a past president of the Central Mississippi Medical Society and a former trustee of the Mississippi State Medical Association.

□



*Commissioner of Insurance George Dale, right, reviews with Dr. John P. Lee of Forest some of his responsibilities as the new appointee to the board of directors of the Mississippi Comprehensive Health Insurance Risk Pool Association. The program is designed to provide health insurance coverage to uninsurable persons. Dr. Lee will represent medical providers on the seven member board.*

**THE DELTA REGION AIDS EDUCATION AND TRAINING CENTER** grant is one of 17 federally funded for specialized comprehensive HIV/AIDS Education and Training in Arkansas, Louisiana, and Mississippi. Educational offerings are available in six disciplines - medicine, nursing, dentistry, infection control, mental health, and social work. Physicians, nurses, and health-related professionals are available to visit your area and provide educational services. Please include us in your next meeting. Additional information may be obtained by calling the Division of Infectious Diseases, University of Mississippi Medical Center.

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# Over 1,100 Mississippi Students Attend Health Choice 93

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On May 31 Health Choice was held for the first time in Columbus, MS with over 450 students participating.



On April 1, Health Choice was held in Hattiesburg, MS for its third year with over 750 students participating.

The facial expressions of the students in the photo at the left and the auxiliary members in the lower photo say it all.

Auxiliary Health Projects Chairman Jeanne Morrison, wife of Dr. William Morrison, an orthopaedic surgeon, of Hattiesburg, spent months contacting the Department of Education, school principals and teachers. Her efforts and those of her committee paid off when bus loads of students arrived at each Health Choice location.

The expansion of the Health Choice program to Columbus provided the opportunity for students in north Mississippi to participate. Auxiliary members from Columbus worked with local teachers and the media to insure good participation and media coverage of this one day event.

Keynote speaker again this year was JeVon Thompson from Olympia, Washington.



The raised hands in the photo at the right are in response to a question from JeVon. He had asked how many of them had an immediate family member or relative that they suspected was addicted to drugs or alcohol.

At the Columbus session over 85% of the students present raised their hands and in Hattiesburg approximately 75% did. His point was to show these students that they are at risk for addiction. His message was that they must never start taking drugs or drinking alcohol.

JeVon also talked about self esteem, developing a positive attitude and success. He has a wonderful rapport with his audience.... he speaks their language both in words and gestures.

Students also had the opportunity to hear the RAP team from the MS Children's Home Society. The team members relate very matter of factly to the audience about sexual abstinence, HIV, alcohol abuse and drug addiction while telling about their own personal experiences.

Plans are already underway for Health Choice '94 and the possibility of having three sessions and even more student participants. This program is presented in support of Comprehensive Health Education. □





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# The University of Mississippi Medical Center

## Medical School Building Dedication Honors First Dean

A building dedication at the University of Mississippi Medical Center will honor one of the major figures in the history of medical education in Mississippi.

The School of Medicine building, a part of the original 1955 construction, will be formally named in a ceremony on Tuesday, April 13, to honor Dr. David S. Pankratz.

Dr. Pankratz was the first dean of the four-year school and first director of the Medical Center.

Ole Miss Chancellor Dr. R. Gerald Turner will preside at the 11 a.m. ceremony under the portico between the medical and nursing school buildings.

Other program participants include UMC vice chancellor Dr. Norman Nelson, Dr. Arthur Guyton, professor emeritus of physiology and biophysics, and Dr. Frank Crosthwait, president of the Board of Trustees, Institutions of Higher Learning.

Howard Duvall, the husband of Geraldine Duvall, the only child of Dr. and Mrs. Pankratz, will make a response from the Pankratz family.

The Duvalls, of Oxford, are the parents of two daughters,

expected to attend the dedication.

Dr. Pankratz served at the Medical Center's helm for six years. At the time of his retirement in 1961, the medical school had earned accreditation, funds were appropriated for a research wing, and four classes of MDs, the first ever trained entirely at home, had graduated.

The Medical Center's completion in 1955 was the culmination of a dream Dr. Pankratz shared with many others, but if any one person could be credited with its establishment, it is Dr. Pankratz, said Chancellor Turner.

Friends, colleagues and former students recognized the importance of his leadership by establishing a scholarship fund in his name at the Medical Center when he died in 1980 at age 82.

In 1939, Dr. Pankratz went to Oxford as professor of anatomy in the two-year medical school, becoming assistant dean in 1945 and dean in 1946.

Mississippi lawmakers passed



Teresa Flautt of Oxford and Ruth Ellen Kuhnelt of Roanoke, Virginia, and grandparents to David Ernest Flautt and Howard Duvall Flautt, both of Oxford. All are

legislation in 1950 authorizing the establishment of the four-year school and teaching hospital in Jackson. "Getting the legislature to vote for the school was a struggle," Dr. Pankratz often said. "But I don't know of any medical school in the country that came easy."

Dr. Pankratz worked with architects and other medical educators to plan the building, and he recruited a young faculty full of promise. "We tried to get native Mississippians who were

making a name for themselves elsewhere to come back and teach. We knew they'd stay longer," he once recalled.

The late University of Mississippi chancellor Dr. John Davis Williams said that Dr. Pankratz' flair for identifying and bringing in aggressive, promising young people was a key element in the Medical Center's rapid growth.

His six years at the helm set the pace for the institution's now traditional quick response to

Mississippi's needs with programs and facilities.

After returning to Oxford in 1972, Dr. Pankratz compiled a history of medical education in Mississippi. That information was included in Lucie R. Bridgforth's *Medical Education in Mississippi*, published by the Medical Alumni Chapter and Guardian Society (Medical Division) of the University of Mississippi Alumni Association in 1984. □

## Dr. Achord Assumes Helm of State ACP

Dr. James L. Achord, professor of medicine and director of digestive diseases, assumed office as governor for the Mississippi Chapter of the American College of Physicians (ACP) during the college's 74th annual session April 1-4 in Washington, DC.

Dr. Achord was elected by ACP-members internists in the Mississippi chapter. ACP is the nation's largest medical specialty society, with more than 80,000 members trained in internal medicine and internal medicine subspecialties.

ACP governors serve as local representatives. They help recruit and credential members, talk with local members for input into college policy making, and direct an annual local scientific meeting. On the national level, the governors advise the ACP Board of Regents.

Dr. Achord was appointed to the UMC faculty in 1976. He received his medical degree from the Emory University School of Medicine. Dr. Achord also interned at Emory where he received postgraduate training in internal medicine and gastroen-

terology. He is a Fellow of the American College of Physicians.

ACP members includes practitioners providing primary care,

medical specialists in fields including cardiology, neurology and oncology, and medical researchers and teachers. □

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**Richmond Alexander, Jr.** of Laurel has completed continuing medical education requirements to retain active membership in the American Academy of Family Physicians.

**Richard Gerald Burris** of Monticello, has completed continuing medical education requirements to retain active membership in the American Academy of Family Physicians.

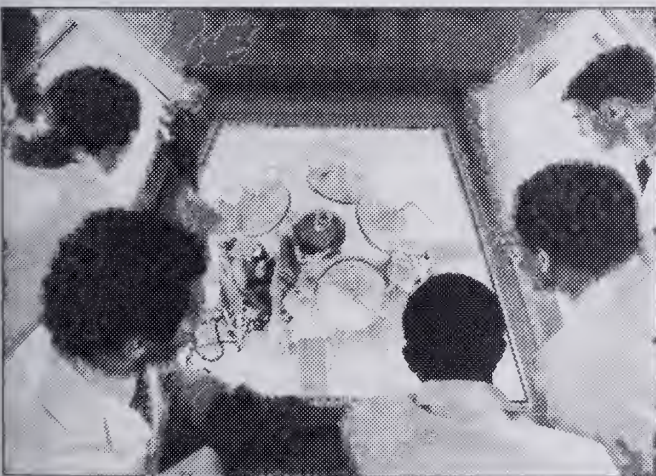
**Walter N. Cosby** announces the opening of his new office at 1107 Earl Frye Boulevard, Suite #3, Amory.

**R. J. Field, Jr** of Centreville, was installed as president of the Southeastern Surgical Congress in February. The Southeastern Surgical Congress is composed of 3,500 surgeons predominately from the southeastern United States. He also served as Visiting Professor at the

University of Alabama School of Medicine in Birmingham. While there he moderated a panel on problems in rural medicine and spoke at Grand Surgical Rounds on the topic *Surgery in Rural America*.

**L. C. Henson** of Kilmichael, has completed continuing medical education requirements to retain active membership in the American Academy of Family Physicians.

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## Personals/*continued*

**Benton Hilbun** of Tupelo presented a paper on *Diagnosis and Management of Mediastinal Masses* at the James D. Hardy Society Meeting in Destin, Florida on April 17.

**J. Martin Lee** of Nephrology & Hypertension Associates, Tupelo, recently passed the Nephrology Subspecialty Board Examination.

**Robert P. Mathis** of Tupelo recently received a three-year appointment as cancer liaison physician for the Hospital Cancer Program at the North Mississippi Medical Center.

**Fred J. McDonnell** of Hazlehurst has completed education requirements to retain active membership in the American Academy of Family Physicians.

**Hugh C. Moore** of Tupelo was recently elected a Fellow of the Royal Society of Medicine, and the Royal College of Pathologists, in London England. He was also elected secretary-treasurer of Blood Systems, Inc., parent corporation of United Blood Services of Mississippi. BSI is headquartered in Scottsdale, AZ.

**F. H. (Buddy) Savoie** of Jackson, presented at the Annual meeting of

the Academy of Orthopaedic Surgeons: A poster and scientific exhibit on *Arthroscopic Capsular Release of Flexion Contractures of the Elbow* with **Scott Jones**. He also gave an instructional course lecture on *Shoulder Arthroscopy with Focus on Arthroscopic Assessment and Treatment of Common Shoulder Disorders* with Live Video Surgical Demonstration. Additionally, he presented a scientific paper on *Carpal Instability with Displaced Intra-Articular Distal Radius* with **Walter B. Geissler, Alan E. Freeland, and Terry Whipple**.

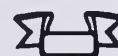
**James C. Waites** of Laurel has been elected president-elect of the newly formed Southern Association for Family Practice (SAFP). The SAFP was established because of the need expressed by physicians practicing in the South to have the opportunity to obtain quality continuing medical education designed especially for family practice physicians facing issues unique to the South.

**Jess Wesberry, Jr.**, a general ophthalmologist and subspecialist in diseases of the retina and vitreous, has associated with **Albert Laws** and has offices in Columbus and Amory. Dr. Wesberry is a diplomate of the American Board of Ophthalmology. □

## Send Items for the Personals Column

to the Editor,  
*Journal MSMA*  
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Jackson, MS  
39296-5229

## Physicians' Recognition Award



Three MSMA members were named recipients of the AMA Physicians Recognition Award in March 1993.

This award is presented by the American Medical Association to Physicians who have voluntarily completed a specified number of continuing medical education hours.

These individuals are presented below by Medical Society.

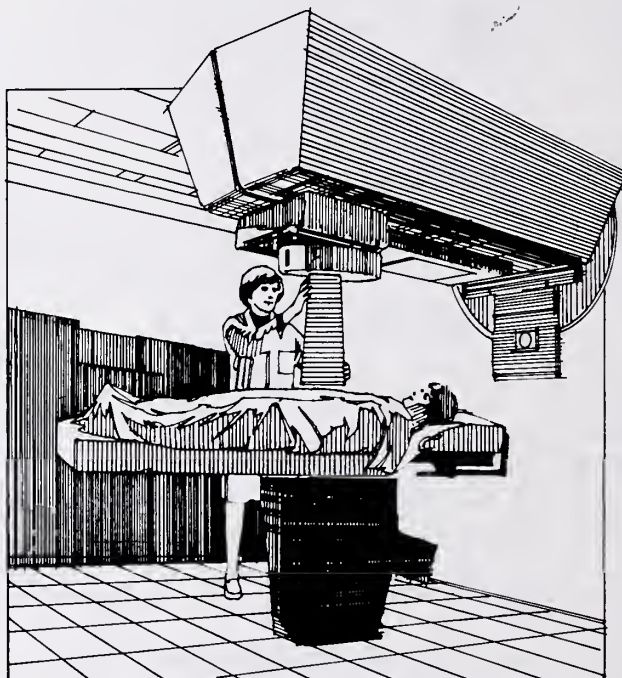
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**Manuscripts** should be of an appropriate length due to the policy of the Journal to feature concise but complete articles. (Some subjects may necessitate exception to this policy and will be reviewed and published at the Editor's discretion.) The language and vocabulary of the manuscript should be understandable and not beyond the comprehension of the general readership of the Journal. The Journal attempts to avoid the use of medical jargon and abbreviations. All abbreviations, especially of laboratory and diagnostic procedures, must be identified in the text. Manuscripts must be typed, double-spaced with adequate margins. (This applies to all manuscript elements including text, references, legends, footnotes, etc.) **The original and one duplicate should be submitted.** The Journal will also accept manuscripts in the form stated above on IBM-compatible floppy diskette. If a diskette accompanies the manuscript, please identify the word processing program used and the file name. Pages should be numbered. An accompanying cover letter should designate one author as correspondent and include his/her address and telephone number. Manuscripts are received with the explicit understanding that they have not been previously published and are not under consideration by any other publication. Manuscripts are subject to editorial revisions as deemed necessary by the editors and to such modifications as to bring them into conformity with Journal style. The authors clearly bear the full responsibility for all statements made and the veracity of the work reported therein.

**Reviewing Process.** Each manuscript is reviewed by the Editor and/or Associate Editor. The acceptability of

a manuscript is determined by such factors as the quality of the manuscript, perceived interest to Journal readers, and usefulness or importance to physicians. Authors are notified upon the acceptance or rejection of their manuscript. Accepted manuscripts become the property of the Journal and may not be published elsewhere, in part or in whole, without permission from the Journal.

**Title Page** should carry [1] the title of the manuscript, which should be concise but informative; [2] full name of each author, with highest academic degree(s), listed in descending order of magnitude of contribution (only the names of those who have contributed materially to the preparation of the manuscript should be included); [3] a one- to two-sentence biographical description for each author which should include specialty, practice location, academic appointments, primary hospital affiliation, or other credits; [4] name and address of author to whom requests for reprints should be addressed, or a statement that reprints will not be available.

**Abstract**, if included, should be on the second page and consist of no more than 150 words. It is designed to acquaint the potential reader with the essence of the text and should be factual and informative rather than descriptive. The abstract should be intelligible when divorced from the article, devoid of undefined abbreviations. The abstract should contain: [1] a brief statement of the manuscript's purpose; [2] the approach used; [3] the material studied; [4] the results obtained. Emphasize new and important aspects of the study or observations. The abstract may be graphically boxed and printed as part of the published manuscript.

**Key Words** should follow the abstract and be identified as such. Provide three to five key words or short phrases that will assist indexers in cross indexing your article. Use terms from the Medical Subject Heading list from Index Medicus when possible.

**Subheads** are strongly encouraged. They should provide guidance for the reader and serve to break the typographic monotony of the text. The format is flexible but subheads ordinarily include: Methods and Materials, Case Reports, Symptoms, Examination, Treatment and Technique, Results, Discussion, and Summary.

**References** must be double spaced on a separate sheet of paper and limited to a reasonable number. They will be critically examined at the time of review and must be kept to a minimum. All references must be cited in the text and the list should be arranged in order of citation, not alphabetically. Personal Communications and unpublished data should not be included in references, but should be incorporated in the text. The following form should be followed:

#### Journals

[1] **Author(s).** Use the surname followed by initial without punctuation. The names of all authors should be given unless there are more than three, in which case the names of the first three authors are used, followed by "et al." [2] **Title of article.** Capitalize only the first letter of the first word. [3] **Name of Journal** followed by no punctuation, underscored or in italics, and abbreviated according to List of Journals Indexed in Index Medicus. [4] **Year of publication;** [5] **Volume number:** Do not include issue number or month except in the case of a supplement or when pagination is not consecutive throughout the volume. [6] **Inclusive page numbers.** Do not omit digits.

**Example:** Bora LI, Dannem FJ, Stanford W, et al. A guideline for blood use during surgery. *Am J Clin Pathol* 1979;71:680-692.

#### Books

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**Example:** DeGole EL, Spann E, Hurst RA Jr, et al. Bedside Examination, in *Cardiovascular Medicine*, ed 2, Smith JT (ed). New York, McGraw Hill Co, 1986, pp 23-27.

**Illustrations** should be submitted in duplicate in an envelope (paper clips should not be used on illustrations since the indentation they make may show on reproduction). Legends should be typed, double-spaced on a separate sheet of paper. Photographic material should be high-contrast glossy prints. Patients must be unrecognizable in photographs unless specific written consent has been obtained, in which case a copy of the authorization should accompany the manuscript. All illustrations should be referred to in the body of the text. Omit illustrations which do not increase understanding of text. **Illustrations must be limited to a reasonable number** (four illustrations should be adequate for a manuscript of 4 to 5 typed pages.) The following information should be typed on a label and affixed to the back of each illustration: figure number, title of manuscript, name of senior author, and arrow indicating top.

**Tables** should be self-explanatory and should supplement, not duplicate, the text. Each should be typed on a separate sheet of paper, be numbered, and have a brief descriptive title.

**Acknowledgments** are the author's prerogative; however, acknowledgment of technicians and other remunerated personnel for carrying out routine operations or of resident physicians who merely care for patients as part of their hospital duties is discouraged. More acceptable acknowledgements include those of intellectual or professional participation. The recognition of assistance should be stated as simply as possible, without effusiveness or superlatives.

**Galley Proofs** will be mailed to the principal author for corrections. Reprint order forms will accompany galley proofs. □



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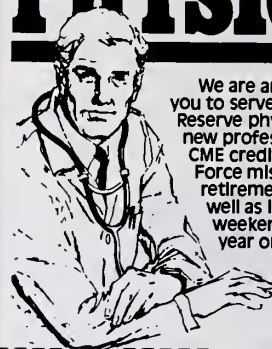
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## Index to Advertisers

Avanti ..... 170

Bristol-Myers Squibb Company -  
Pravachol ..... **third and fourth cover**

CancerPay Plus ..... 172  
CompHealth ..... 158

Disability Determination ..... 175  
Doctors Insurance Reciprocal ..... 152

Eli Lilly & Co. - Humulin ..... **6**  
Employer Plus, Inc. .... 159

Medical Assurance Co. of MS ..... **second cover**  
MS Emergency Association ..... 175  
MS Physicians Insurance Company ..... 153  
MSMA Benefit Plan & Trust ..... 163

Opportunity Hotline ..... 176

Palisades Pharmaceuticals, Inc. - Yocon ..... 156  
Premier Printing ..... 168  
PRI-MED, Inc. .... 177

The Doctors' Company ..... 166  
Trustmark ..... 156

US Air Force Reserve ..... 176  
US Army Active ..... 169  
US Army Reserve ..... 151



## CONTRAINDICATIONS

-hypersensitivity to any component of this medication.

Active liver disease or unexplained, persistent elevations in liver function tests (see WARNINGS).

**Pregnancy and lactation.** Atherosclerosis is a chronic process and discontinuation of lipid-lowering drugs during pregnancy should have little impact on the outcome of long-term therapy of primary hypercholesterolemia. Cholesterol and other products of cholesterol biosynthesis are essential components for fetal development (including synthesis of steroids and cell membranes). Since HMG-CoA reductase inhibitors decrease cholesterol synthesis and possibly the synthesis of other biologically active substances derived from cholesterol, they may cause fetal harm when administered to pregnant women. Therefore, HMG-CoA reductase inhibitors are contraindicated during pregnancy and in nursing mothers. **Pravastatin should be administered to women of childbearing age only when such patients are highly unlikely to conceive and have been informed of the potential hazards.** If the patient becomes pregnant while taking this class of drug, therapy should be discontinued and the patient apprised of the potential hazard to the fetus.

## WARNINGS

**Liver Enzymes:** HMG-CoA reductase inhibitors, like some other lipid-lowering therapies, have been associated with biochemical abnormalities of liver function. Increases of serum transaminase (ALT, AST) values to more than 3 times the upper limit of normal occurring on 2 or more (not necessarily sequential) occasions have been reported in 1.3% of patients treated with pravastatin in the U.S. over an average period of 18 months. These abnormalities were not associated with cholestasis and did not appear to be related to treatment duration. In those patients in whom these abnormalities were believed to be related to pravastatin and who were discontinued from therapy, the transaminase levels usually fell slowly to pretreatment levels. These biochemical findings are usually symptomatic although worldwide experience indicates that anorexia, weakness, and/or abdominal pain may also be present in rare patients.

As with other lipid-lowering agents, liver function tests should be performed during therapy with pravastatin. Serum aminotransferases, including ALT (SGPT), should be monitored before treatment begins, every six weeks for the first three months, every eight weeks during the remainder of the first year, and periodically thereafter (e.g., at about six-month intervals). Special attention should be given to patients who develop increased transaminase levels. Liver function tests should be repeated to confirm an elevation and subsequently monitored at more frequent intervals. If increases in AST and ALT equal or exceed three times the upper limit of normal and persist, then therapy should be discontinued. Persistence of significant aminotransferase elevations following discontinuation of therapy may warrant consideration of liver biopsy.

Active liver disease or unexplained transaminase elevations are contraindications to the use of pravastatin (see CONTRAINDICATIONS). Caution should be exercised when pravastatin is administered to patients with a history of liver disease or heavy alcohol ingestion (see CLINICAL PHARMACOLOGY: Pharmacokinetics/Metabolism). Such patients should be closely monitored, started at the lower end of the recommended dosing range, and titrated to the desired therapeutic effect.

**Skeletal Muscle:** Rhabdomyolysis with renal dysfunction secondary to myoglobinuria has been reported with pravastatin and other drugs in this class. Uncomplicated myalgia has also been reported in pravastatin-treated patients (see ADVERSE REACTIONS). Myopathy, defined as muscle aching or muscle weakness in conjunction with increases in creatine phosphokinase (CPK) values to greater than 10 times the upper limit of normal was reported to be possibly due to pravastatin in only one patient in clinical trials (<0.1%). Myopathy should be considered in any patient with diffuse myalgias, muscle tenderness or weakness, and/or marked elevation of CPK. Patients should be advised to report promptly unexplained muscle pain, tenderness or weakness, particularly if accompanied by malaise or fever. **Pravastatin therapy should be discontinued if markedly elevated CPK levels occur or myopathy is diagnosed or suspected. Pravastatin therapy should also be temporarily withheld in any patient experiencing an acute or serious condition predisposing to the development of renal failure secondary to rhabdomyolysis, e.g., sepsis; hypotension; major surgery; trauma; severe metabolic, endocrine, or electrolyte disorders; or uncontrolled epilepsy.**

The risk of myopathy during treatment with lovastatin is increased if therapy with either cyclosporine, gemfibrozil, erythromycin, or niacin is administered concurrently. There is no experience with the use of pravastatin together with cyclosporine. Myopathy has not been observed in clinical trials involving small numbers of patients who were treated with pravastatin together with niacin. One trial of limited size involving combined therapy with pravastatin and gemfibrozil showed a trend toward more frequent CPK elevations and patient withdrawals due to musculoskeletal symptoms in the group receiving combined treatment as compared with the groups receiving placebo, gemfibrozil, or pravastatin monotherapy. Myopathy was not reported in this trial (see PRECAUTIONS: Drug Interactions). One patient developed myopathy when clofibrate was added to a previously well tolerated regimen of pravastatin; the myopathy resolved when clofibrate therapy was stopped and pravastatin treatment continued. **The use of fibrates alone may occasionally be associated with myopathy. The combined use of pravastatin and fibrates should generally be avoided.**

## PRECAUTIONS

**General:** Pravastatin may elevate creatine phosphokinase and transaminase levels (see ADVERSE REACTIONS). This should be considered in the differential diagnosis of chest pain in a patient on therapy with pravastatin.

**Homozygous Familial Hypercholesterolemia.** Pravastatin has not been evaluated in patients with rare homozygous familial hypercholesterolemia. In this group of patients, it has been reported that HMG-CoA reductase inhibitors are less effective because the patients lack functional LDL receptors.

**Renal Insufficiency:** A single 20 mg oral dose of pravastatin was administered to 24 patients with varying degrees of renal impairment (as determined by creatinine clearance). No effect was observed on the pharmacokinetics of pravastatin or its 3 $\alpha$ -hydroxy isomeric metabolite (SQ 31,906). A small increase was seen in mean AUC values and half-life (t<sub>1/2</sub>) for the inactive enzymatic ring hydroxylation metabolite (SQ 31,945). Given this small sample size, the dosage administered, and the degree of individual variability, patients with renal impairment who are receiving pravastatin should be closely monitored.

**Information for Patients:** Patients should be advised to report promptly unexplained muscle pain, tenderness or weakness, particularly if accompanied by malaise or fever.

**Drug Interactions:** Immunosuppressive Drugs, Gemfibrozil, Niacin (Nicotinic Acid), Erythromycin: See WARNINGS: Skeletal Muscle.

**Antipyrine:** Clearance by the cytochrome P450 system was unaltered by concomitant administration of pravastatin. Since pravastatin does not appear to induce hepatic drug-metabolizing enzymes, it is not expected that any significant interaction of pravastatin with other drugs (e.g., phenytoin, quinidine) metabolized by the cytochrome P450 system will occur.

**Cholestyramine/Colestipol:** Concomitant administration resulted in an approximately 40 to 50% decrease in the mean AUC of pravastatin. However, when pravastatin was administered 1 hour before or 4 hours after cholestyramine or 1 hour before colestipol and a standard meal, there was no clinically significant decrease in bioavailability or therapeutic effect. (See DOSAGE AND ADMINISTRATION: Concomitant Therapy.)

**Warfarin:** In a study involving 10 healthy male subjects given pravastatin and warfarin concomitantly for 6 days, bioavailability parameters at steady state for pravastatin (parent compound) were not altered. Pravastatin did not alter the plasma protein-binding of warfarin. Concomitant dosing did increase the AUC and C<sub>max</sub> of warfarin but did not produce any changes in its anticoagulant action (i.e., no increase was seen in mean prothrombin time after 6 days of concomitant therapy). However, bleeding and extreme prolongation of prothrombin time has been reported with another drug in this class. Patients receiving warfarin-type anticoagulants should have their prothrombin times closely monitored when pravastatin is initiated or the dosage of pravastatin is changed.

**Cimetidine:** The AUC<sub>0-12h</sub> for pravastatin when given with cimetidine was not significantly different from the AUC for pravastatin when given alone. A significant difference was observed between the AUC's for pravastatin when given with cimetidine compared to when administered with antacid.

**Digoxin:** In a crossover trial involving 18 healthy male subjects given pravastatin and digoxin concurrently for 9 days, the bioavailability parameters of digoxin were not affected. The AUC of pravastatin tended to increase, but the overall bioavailability of pravastatin plus its metabolites SQ 31,906 and SQ 31,945 was not altered.

**Gemfibrozil:** In a crossover study in 20 healthy male volunteers given concomitant single doses of pravastatin and gemfibrozil, there was a significant decrease in urinary excretion and protein binding of pravastatin. In addition, there was a significant increase in AUC, C<sub>max</sub>, and t<sub>max</sub> for the pravastatin metabolite SQ 31,906. Combination therapy with pravastatin and gemfibrozil is generally not recommended.

In interaction studies with aspirin, antacids (1 hour prior to PRAVACHOL), cimetidine, nicotinic acid, or probucol, no statistically significant differences in bioavailability were seen when PRAVACHOL (pravastatin sodium) was administered.

**Other Drugs:** During clinical trials, no noticeable drug interactions were reported when PRAVACHOL was added to: diuretics, antihypertensives, digitalis, converting-enzyme inhibitors, calcium channel blockers, beta-blockers, or nitroglycerin.

**Endocrine Function:** HMG-CoA reductase inhibitors interfere with cholesterol synthesis and lower circulating cholesterol levels and, as such, might theoretically blunt adrenal or gonadal steroid hormone production. Results of clinical trials with pravastatin in males and post-menopausal females were inconsistent with regard to possible effects of the drug on basal steroid hormone levels. In a study of 21 males, the mean testosterone response to human chorionic gonadotropin was significantly reduced (p<0.004) after 16 weeks of treatment with 40 mg of pravastatin. However, the percentage of patients showing a  $\geq$ 50% rise in plasma testosterone after human chorionic gonadotropin stimulation did not change significantly after therapy in these patients. The effects of HMG-CoA reductase inhibitors on spermatogenesis and fertility have not been studied in adequate numbers of patients. The effects, if any, of pravastatin on the pituitary-gonadal axis in pre-menopausal females are unknown. Patients treated with pravastatin who display clinical evidence of endocrine dysfunction should be evaluated appropriately. Caution should also be exercised if an HMG-CoA reductase inhibitor or other agent used to lower cholesterol levels is administered to patients also receiving other drugs (e.g., ketoconazole, spironolactone, cimetidine) that may diminish the levels or activity of steroid hormones.

**CNS Toxicity:** CNS vascular lesions, characterized by perivascular hemorrhage and edema and mononuclear cell infiltration of perivascular spaces, were seen in dogs treated with pravastatin at a dose of 25 mg/kg/day, a dose that produced a plasma drug level about 50 times higher than the mean drug level in humans taking 40 mg/day. Similar CNS vascular lesions have been observed with several other drugs in this class.

A chemically similar drug in this class produced optic nerve degeneration (Wallenian degeneration of reti-

na) in clinically normal dogs in a dose-dependent fashion starting at 60 mg/kg/day, a dose that produced mean plasma drug levels about 30 times higher than the mean drug level in humans taking the highest recommended dose (as measured by total enzyme inhibitory activity). This same drug also produced vestibulocochlear Wallenian-like degeneration and retinal ganglion cell chromatolysis in dogs treated for 14 weeks at 180 mg/kg/day, a dose which resulted in a mean plasma drug level similar to that seen with the 60 mg/kg/day dose.

**Carcinogenesis, Mutagenesis, Impairment of Fertility:** In a 2-year study in rats fed pravastatin at doses of 10, 30, or 100 mg/kg body weight, there was an increased incidence of hepatocellular carcinomas in males at the highest dose (p<0.01). Although rats were given up to 125 times the human dose (HD) on a mg/kg body weight basis, their serum drug levels were only 6 to 10 times higher than those measured in humans given 40 mg pravastatin as measured by AUC.

The oral administration of 10, 30, or 100 mg/kg (producing plasma drug levels approximately 0.5 to 5.0 times human drug levels at 40 mg) of pravastatin to mice for 22 months resulted in a statistically significant increase in the incidence of malignant lymphomas in treated females when all treatment groups were pooled and compared to controls (p<0.05). The incidence was not dose-related and male mice were not affected.

A chemically similar drug in this class was administered to mice for 72 weeks at 25, 100, and 400 mg/kg body weight, which resulted in mean serum drug levels approximately 3, 15, and 33 times higher than the mean human serum drug concentration (as total inhibitory activity) after a 40 mg oral dose. Liver carcinomas were significantly increased in high-dose females and mid- and high-dose males, with a maximum incidence of 90 percent in males. The incidence of adenomas of the liver was significantly increased in mid- and high-dose females. Drug treatment also significantly increased the incidence of lung adenomas in mid- and high-dose males and females. Adenomas of the eye (Harderian gland (a gland of the eye of rodents)) were significantly higher in high-dose mice than in controls.

No evidence of mutagenicity was observed *in vitro*, with or without rat-liver metabolic activation, in the following studies: microbial mutagen tests, using mutant strains of *Salmonella typhimurium* or *Escherichia coli*; a forward mutation assay in L5178Y TK +/– mouse lymphoma cells; a chromosomal aberration test in hamster cells; and a gene conversion assay using *Saccharomyces cerevisiae*. In addition, there was no evidence of mutagenicity in either a dominant lethal test in mice or a micronucleus test in mice.

In a study in rats, with daily doses up to 500 mg/kg, pravastatin did not produce any adverse effects on fertility or general reproductive performance. However, in a study with another HMG-CoA reductase inhibitor, there was decreased fertility in male rats treated for 34 weeks at 25 mg/kg body weight, although this effect was not observed in a subsequent fertility study when this same dose was administered for 11 weeks (the entire cycle of spermatogenesis, including epididymal maturation). In rats treated with this same reductase inhibitor at 180 mg/kg/day, seminiferous tubule degeneration (necrosis and loss of spermatogenic epithelium) was observed. Although not seen with pravastatin, two similar drugs in this class caused drug-related testicular atrophy, decreased spermatogenesis, spermatocytic degeneration, and giant cell formation in dogs. The clinical significance of these findings is unclear.

**Pregnancy: Pregnancy Category X:** See CONTRAINDICATIONS.

Safety in pregnant women has not been established. Pravastatin was not teratogenic in rats at doses up to 1000 mg/kg daily or in rabbits at doses of up to 50 mg/kg daily. These doses resulted in 20x (rabbit) or 240x (rat) the human exposure based on surface area (mg/meter<sup>2</sup>). However, in studies with another HMG-CoA reductase inhibitor, skeletal malformations were observed in rats and mice. PRAVACHOL (pravastatin sodium) should be administered to women of child-bearing potential only when such patients are highly unlikely to conceive and have been informed of the potential hazards. If the woman becomes pregnant while taking PRAVACHOL (pravastatin sodium), it should be discontinued and the patient advised again as to the potential hazards to the fetus.

**Nursing Mothers:** A small amount of pravastatin is excreted in human breast milk. Because of the potential for serious adverse reactions in nursing infants, women taking PRAVACHOL should not nurse (see CONTRAINDICATIONS).

**Pediatric Use:** Safety and effectiveness in individuals less than 18 years old have not been established. Hence, treatment in patients less than 18 years old is not recommended at this time. (See also PRECAUTIONS: General.)

## ADVERSE REACTIONS

Pravastatin is generally well tolerated; adverse reactions have usually been mild and transient. In 4-month long placebo-controlled trials, 1.7% of pravastatin-treated patients and 1.2% of placebo-treated patients were discontinued from treatment because of adverse experiences attributed to study drug therapy; this difference was not statistically significant. In long-term studies, the most common reasons for discontinuation were asymptomatic serum transaminase increases and mild, non-specific gastrointestinal complaints. During clinical trials the overall incidence of adverse events in the elderly was not different from the incidence observed in younger patients.

**Adverse Clinical Events:** All adverse clinical events (regardless of attribution) reported in more than 2% of pravastatin-treated patients in the placebo-controlled trials are identified in the table below; also shown are the percentages of patients in whom these medical events were believed to be related or possibly related to the drug:

Body System/Event	All Events %		Events Attributed to Study Drug %	
	Pravastatin (N=900)	Placebo (N=411)	Pravastatin (N=900)	Placebo (N=411)
Cardiovascular				
Cardiac Chest Pain	4.0	3.4	0.1	0.0
Dermatologic				
Rash	4.0*	1.1	1.3	0.9
Gastrointestinal				
Nausea/Vomiting	7.3	7.1	2.9	3.4
Diarrhea	6.2	5.6	2.0	1.9
Abdominal Pain	5.4	6.9	2.0	3.9
Constipation	4.0	7.1	2.4	5.1
Flatulence	3.3	3.6	2.7	3.4
Heartburn	2.9	1.9	2.0	0.7
General				
Fatigue	3.8	3.4	1.9	1.0
Chest Pain	3.7	1.9	0.3	0.2
Influenza	2.4*	0.7	0.0	0.0
Musculoskeletal				
Localized Pain	10.0	9.0	1.4	1.5
Myalgia	2.7	1.0	0.6	0.0
Nervous System				
Headache	6.2	3.9	1.7*	0.2
Dizziness	3.3	3.2	1.0	0.5
Renal/Genitourinary				
Urinary Abnormality	2.4	2.9	0.7	1.2
Respiratory				
Common Cold	7.0	6.3	0.0	0.0
Rhinitis	4.0	4.1	0.1	0.0
Cough	2.6	1.7	0.1	0.0

\*Statistically significantly different from placebo.

The following effects have been reported with drugs in this class.

**Skeletal:** myopathy, rhabdomyolysis.

**Neurological:** dysfunction of certain cranial nerves (including alteration of taste, impairment of extra-ocular movement, facial paresis), tremor, vertigo, memory loss, paresthesia, peripheral neuropathy, peripheral nerve palsy.

**Hypersensitivity Reactions:** An apparent hypersensitivity syndrome has been reported rarely which has included one or more of the following features: anaphylaxis, angioedema, lupus erythematosus-like syndrome, polymyalgia rheumatica, vasculitis, purpura, thrombocytopenia, leukopenia, hemolytic anemia, positive ANA, ESR increase, arthritis, arthralgia, urticaria, asthenia, photosensitivity, fever, chills, flushing, malaise, dyspnea, toxic epidermal necrolysis, erythema multiforme, including Stevens-Johnson syndrome.

**Gastrointestinal:** pancreatitis, hepatitis, including chronic active hepatitis, cholestatic jaundice, fatty change in liver, and, rarely, cirrhosis, fulminant hepatic necrosis, and hepatoma, anorexia, vomiting.

**Reproductive:** gynecomastia, loss of libido, erectile dysfunction.

**Eye:** progression of cataracts (lens opacities), ophthalmoplegia.

**Laboratory Test Abnormalities:** Increases in serum transaminase (ALT, AST) values and CPK have been observed (see WARNINGS).

Transient, asymptomatic eosinophilia has been reported. Eosinophil counts usually returned to normal despite continued therapy. Anemia, thrombocytopenia, and leukopenia have been reported with other HMG-CoA reductase inhibitors.

**Concomitant Therapy:** Pravastatin has been administered concurrently with cholestyramine, colestipol, nicotinic acid, probucol and gemfibrozil. Preliminary data suggest that the addition of either probucol or gemfibrozil to therapy with lovastatin or pravastatin is **not** associated with greater reduction in LDL cholesterol than that achieved with lovastatin or pravastatin alone. No adverse reactions unique to the combination or in addition to those previously reported for each drug alone have been reported. Myopathy and rhabdomyolysis (with or without acute renal failure) have been reported when another HMG-CoA reductase inhibitor was used in combination with immunosuppressive drugs, gemfibrozil, erythromycin, or lipid-lowering doses of nicotinic acid. Concomitant therapy with HMG-CoA reductase inhibitors and these agents is generally not recommended. (See WARNINGS: Skeletal Muscle and PRECAUTIONS: Drug Interactions.)

## OVERDOSAGE

There have been no reports of overdoses with pravastatin.

Should an accidental overdose occur, treat symptomatically and institute supportive measures as required (J4-422A)



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JUNE 1993

VOLUME XXXIV

NUMBER 6

## SCIENTIFIC ARTICLES

- Common Patient Symptoms: Patterns of Self-Treatment and Prevention** 179

*George E. Habeeb, Jr., MD and  
Judith G. Gearhart, MD*

- The Bacteriology Of Chronic Sinusitis In Pediatrics** 183

*Tara Sturdivant, MD and C. Ron Cannon, MD*

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## SPECIAL ARTICLE

- Address of the President** 187

*William C. Gates, Jr., MD*

## EDITORIALS

- A Level Playing Field** 192

*Don Q. Mitchell, MD*

- Overall Physician Cost Effectiveness** 193

*George E. Abraham, MD, Associate Editor*

## DEPARTMENTS

- Comments** 195  
**Medical Organization** 198  
**New Members** 210  
**Deaths** 212  
**Personals** 214  
**Placement Service** 220  
**Classified** 222

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**C. Stratton Hill, Jr., M.D.**  
**of**  
**M.D. Anderson Cancer Center in**  
**Houston, Texas**  
**will speak on**  
**PAIN MANAGEMENT**  
**at the**  
**Mississippi Baptist**  
**Medical Center**  
**on**  
**July 7, 1993**  
**at noon**  
**in the John Busey Auditorium**

C. Stratton Hill, Jr., M.D. is Professor of Medicine in the Department of Neuro-Oncology at the University of Texas, M.D. Anderson Cancer Center in Houston. He is also an internist at the University's cancer center.

Dr. Hill is a member of several medical and scientific societies such as the American Medical Association, the American Society of Clinical Oncology, and the International Association for the Study of Pain. He is also a member of the Ad Hoc Committee on Pain Relief of American Society of Clinical Oncology and the Advisory Committee on

Pain Relief of the American Cancer Society National Office.

Dr. Hill serves on the editorial board of three professional journals: Cancer Bulletin, Year Book of Cancer, and Pain Clinic Journal. He has been published in more than 30 publications including Cancer and The New England Journal of Medicine.

Dr. Hill received his MD from the University of Tennessee's College of Medicine.

*For more information:*

Contact Linda Edwards of Hospice of Central Mississippi at 366-9881 or 1/800/273-7724.



# Dateline

Journal of the Mississippi State Medical Association  
Volume XXXIV, Number 6

## Sta-home Receives JCAHO Accreditation

Jackson, MS - Sta-home Health Agency, Inc. recently became the first free-standing home health agency in Mississippi to be accredited by the Joint Commission on Accreditation of Healthcare Organizations (JCAHO), the nation's largest voluntary accrediting body in health care. The agency received full three-year accreditation with commendation, effective February 2 of this year.

According to Sta-home Chief Executive Officer Michael Caracci, "With so many home care agencies offering services, we believed it essential to gain accreditation to assure the communities and physicians we serve, that we subscribe to the highest standards of care." Sta-home is one of approximately 1,100 free-standing home care agencies nationwide to be accredited by JCAHO.

The purpose of the accreditation process is to promote quality home care through an objective assessment of the home care organization and the care provided to patients. Home care makes it possible for people to receive a full range of health care services in their own home, under the direction of a physician.

Accreditation involves an intensive survey designed to evaluate all processes involved in the delivery of care to patients. Survey activities, performed by experienced health care professionals, include home visits to patients with staff, home and telephone interviews of patients and caregivers, and a review of records and documentation. In addition, surveyors review administrative and clinical policies, training and education procedures, and the quality assurance program.

With 22 offices serving 19 counties, Sta-home is one of the largest home care agencies in the state. The agency was established in 1976 and provides a full range of services to patients of all ages.

\*\*\*

## Second Conference on Domestic Violence Scheduled

Jackson, MS — *Family Violence and Sexual Assault - The Health Care Response*, the second annual conference on domestic violence sponsored by the Mississippi State Coalition Against Domestic Violence will be held at the Ramada Coliseum, Jackson, MS, August 26-27, 1993. The *Journal MSMA* will print further registration information as it becomes available.

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# Common Patient Symptoms: Patterns of Self-Treatment and Prevention

GEORGE E. HABEEB, JR, MD  
JUDITH G. GEARHART, MD

**S**elf-treatment is a common and often necessary part of health care. In a 1987 study the author stated that 50 years ago most disease was acute, but today 80% of all disease is chronic.<sup>1</sup> Therefore, many people may engage in self treatment. Self-treatment is practiced by about 80% of people in industrialized nations.<sup>2</sup> Every day, 60% of the people in the U.S. and United Kingdom are taking either prescription or non-prescription medicines.<sup>3</sup> In a survey of 2603 magazine subscribers, 90% stated that they use over-the-counter medicines.<sup>4</sup>

The average frequency of an illness episode is about once every four days.<sup>5</sup> The majority of symptoms are not treated by health professionals.<sup>6,7</sup> About 70% to 95% of all self-recognized illness episodes are managed outside the formal health care system.<sup>3,5,8,9</sup> Having compared adults who self-medicate to those who consult a health professional concerning common

**Self treatment is a common and often necessary part of health care. Factors influencing self-treatment include patient satisfaction, cost, educational level, socio-economic factors, age, and gender. In this article, patients' choices of self-treatment are reviewed; the benefits and risks of self-treatment are discussed. One benefit may be decreased health care cost. Risks include drug interactions between prescription and non-prescription drugs. Physicians should be aware that the majority of illness is treated outside the formal health care system. Education is needed to help patients discern whether self-treatment or medical consultation is appropriate.**

symptoms, one author found that the ratio was four to one, respectively.<sup>1</sup>

Using a non-prescription medicine is the initial response in nearly half of treatments for symptoms considered not serious.<sup>7</sup> Similarly, the most frequent response is either a non-prescription or prescription medicine.<sup>5</sup> About 70% to 93% of adult symptoms are managed by self-medication.<sup>4,5,9</sup>

## **SATISFACTION FROM SELF-TREATMENT**

The main reason for one to engage in self-care is that it gives a person a feeling of independence, self-reliance, responsibility, security, and control over one's health. A person gains even more confidence and continues self-care when the treatment is successful. In one survey 92% of the respondents said they were satisfied with the OTC

drugs they used, and 93% said they would use the same OTC drug for a similar problem.<sup>6</sup> In another study 94% of people who used non-prescription medicines thought their treatment was effective.<sup>5</sup> Self-care often alleviates symptoms and improves one's outlook.

In one study, doctors rated the appropriateness of patients' self-treatment choices. Left-over medicines and OTC medicines had the most unfavorable ratings by doctors. However, patient satisfaction was greatest with the use of an OTC medicine.<sup>6</sup>

### **FACTORS INFLUENCING SELF-CARE**

Factors that are associated with self-care include costs, education, socio-economic status, household size, environment, age, sex, nature of symptom, and mass media.

**Costs.** Self-care tends to lower the cost of health care. Lay care, if performed properly, lowers health-care costs and promotes self-reliance.<sup>6</sup> If self-medicators discontinued use of their OTC medicines, then doctors' office visits would be increased. In one study, a self-care medication program in industry was undertaken. Results showed that self-care with OTC products reduced costs by 9%, reduced non-occupational visits to a nurse by 50% to 70%, reduced visiting time, and had few complications over a two year period.<sup>10</sup> Fry states that the demand on health professionals would be doubled without self-care.<sup>3</sup>

**Educational level.** In a study conducted in Singapore, people with higher levels of education had positive correlations with self-medication, the use of modern medicines, knowledge of disease, prevention-orientation, and exposure to mass media.<sup>11</sup> Those

with lower levels of education had negative correlations with these and positive correlations with use of traditional medicines and treatment-orientation.<sup>11</sup> Self-medication behavior may involve the altered use of prescribed medicines especially among those with higher levels of education, although people have greater access to non-prescription medicines.<sup>5</sup> Self-medication is more prevalent among those highly educated.<sup>5,12,13</sup> Those people in a higher social status are more often self-medicators.

**Socio-economic status.** People in larger households tend to self-medicate more often. They are prone to share leftover prescription medicines with each other.<sup>5</sup> Self-medication with non-prescription medicines has also been associated with single person households.<sup>7</sup> People who live in third world nations tend to self-medicate often because of the large population density, scarce food supply, and less availability of health professionals.<sup>14</sup>

**Age.** Some older adults who self-medicate may have less trust in formal medical care. Older women use more medication than older men, report more symptoms, and have more chronic disease. Older men are more often skeptical concerning medical care. Skeptics use OTC medicines more often than prescription medicines. In older people, OTC medicine use may be a daily habit rather than an intervention. In the elderly, self-medication reinforces self-sufficiency.<sup>7</sup>

At least two authors have addressed the subject of age related use of OTC medicines as a substitute for consultation with a health professional. In people under 65 years of age, OTC medicines are used in conjunction with formal medical care and are

not a substitute for it.<sup>12</sup> In persons greater than age 65, self-medication with OTC medicine is usually the first step in an illness but not a substitute for physician consultation.<sup>7</sup>

**Sex.** Comparisons between males and females concerning self medication have yielded different results. One author stated that sex is not a factor in self-medication. Another stated that women use more medications than men.<sup>7</sup> However, in a study of people under 65 years of age, men spent a large portion of their medicine budget on OTC products.<sup>12</sup>

### **PATTERNS OF SELF CARE**

Some common symptoms which are often managed via self care include colds, cough, allergy, sinus trouble, headaches, backaches, upset stomach, constipation, diarrhea, insomnia, and anxiety.<sup>15</sup> The immediate course of action in self treatment for common symptoms may include: change in diet, exercise, relaxation, use of a non-prescription medicine, use of an old or leftover prescription, use of a home remedy, consultation with a doctor or pharmacist, or no action. The course of action for preventing common symptoms could include the same choices. In one study, the most frequently reported medicines in households included headache pills (92.9%), cough medicines (81.6%), vitamins (72.1%), laxatives (50%), tranquilizers (20%), sleeping pills (15-18%).<sup>5</sup> In one study, 77% of medicines used for recent symptoms were already in the household.<sup>5</sup>

### **RISKS OF SELF-MEDICATION**

Self-medication increases the



risk of drug interactions when patients do not inform doctors about OTC medicine use.<sup>7</sup> Improper self-medication with OTC drugs can cause drug interactions and can extend a worker's recovery time. For example, certain OTC medicines for GI disturbances that may interfere with other prescription drugs become a potential source of morbidity.<sup>16</sup> Also, people may not be aware that certain common illnesses are symptoms of underlying disease which may be masked by self-medication.<sup>14</sup>

CONCLUSION

During the past fifty years, advances in medicine and pharmacology have shifted the majority of disease processes from acute to chronic and have shifted more medications from "prescription" to "over-the-counter". Thus, more responsibility is placed on the patient with a common symptom who attempts to engage in self-treatment.

As discussed, the factors influencing self-care include a feeling of self-reliance, economics, educational level, age, sex, and socio-economic status. The main positive factor is that self-care reduces the cost of health care. There appear to be three main negative factors. First, the patient may not be aware of potential drug interactions between prescription and non-prescription medication. Second, the patient may be treating a preventable illness. Third, he/she may be masking a more severe disease.

Primary care physicians should have an increased awareness that the vast majority of illness episodes are handled outside the formal health care system. Patient education is of paramount importance to help the patient discern whether an ailment

warrants prevention, treatment by self-care, or medical consultation. □

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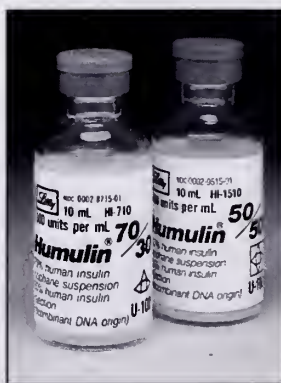
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# The Bacteriology Of Chronic Sinusitis In Pediatrics

TARA STURDIVANT, MD  
C. RON CANNON, MD

Family physicians are often presented with a child who has a history of purulent rhinorrhea and/or cough. In fact, it has been estimated that children suffer from 6 to 8 respiratory tract infections a year. Up to 5% of these are complicated by sinusitis.<sup>1</sup>

Although rarely life-threatening, sinusitis can cause considerable morbidity including reactive airway disease and lower respiratory tract infection.<sup>2</sup> If unrecognized or managed inappropriately, infections can progress to orbital cellulitis and abscess, brain abscess, meningitis, subdural empyema, cranial osteomyelitis, or cavernous sinus thrombosis.<sup>3,4</sup>

Prior research has identified the most common organisms in acute pediatric sinusitis as *Streptococcus pneumoniae*, *Haemophilus influenzae*, and *Moraxella (Branhamella) catarrhalis*.<sup>5,6,7</sup> However, there is limited information on the microbiology of chronic infection in children.<sup>8,2</sup> Previous studies have shown that anaerobes play a predominant role in persistent sinusitis in adults and adolescents.<sup>9,10</sup> Similar findings have not been consistent in children. Feigin and Cherry<sup>6</sup> cite *H. influenzae* and *S. pneumoniae* as primary pathogens in children, with anaerobes playing only a limited role.

Brook,<sup>3,11</sup> however, reported a higher percentage of anaerobic isolates in culture-positive aspirates (100%). The purpose of this retrospective study was to identify the most common pathogens in a sample of pediatric patients undergoing sinus surgery for chronic disease.

## METHOD

### Participants

Intraoperative sinus aspiration and culture of the aspirate were performed on 25 patients ranging in age from 1 to 11 years with a median age of 4.2 years. There were 13 males and 12 females included. Patients had historical, clinical, and radiological evidence of chronic sinusitis and were referred by their primary care physicians for surgical evaluation.

A historical and physical evaluation was made of each subject. Radiological assessment was based on computed tomography (CT) in the coronal plane.<sup>4</sup> These views were obtained in order to demonstrate anatomy from the surgeon's perspective.<sup>12</sup> Disease was ascertained by the presence of sinus opacification, mucosal thickening, air/fluid levels, and patency of the osteomeatal complex.<sup>13</sup> The decision to proceed with surgical treatment was based on the

severity of symptoms and extent of disease on CT scan.

### Procedure

Functional endoscopic sinus surgery was performed using rigid telescopes. General anesthesia was employed in all procedures. Nasal decongestion was obtained with 4% cocaine pledgets after mucosal infiltration of each middle turbinate with 1% xylocaine with 1:100,000 epinephrine. The patients' middle turbinates were fractured medially with a Freer dissector. An incision was made in the ethmoid infundibulum, and an ethmoidectomy was performed under direct vision using a 0 degree telescope, straight suction tip, and straight pituitary forceps. The ostia of each maxillary sinus was identified using a curved suction tip. Specimens were then obtained by direct sinus aspiration through the ostia into a Lukens trap. The natural sinus ostia were then enlarged using back-biting forceps. The operative sites were filled with cortisporin ointment and the procedure terminated.

After transfer of the specimen from the surgical suite to a laboratory facility, aerobic and anaerobic media were employed for culture. Sheep's blood, MacConkey's and chocolate agars, as well as thioglycolate

broth, were inoculated and incubated at 37 degrees celsius aerobically. Plates were read at 24 and 48 hours. Anaerobic media employed were sheep's blood, sheep's blood with kanamycin sulfate (75 mcg/mL) and vancomycin hydrochloride (7.5 mcg/mL), sheep's blood with anaerobic phenyl ethyl alcohol and sheep's blood with colistin-nalidixic acid. Plates were incubated in anaerobic jars and read at 48 and 72 hours. Organisms were identified by standard methods.

## RESULTS

In this series, there were 35 positive cultures with 11 different isolates. The most common pathogens were *Streptococcus pneumoniae* (7), *Haemophilus influenzae* (7), *Staphylococcus aureus* (6), and *Moraxella catarrhalis* (5). Only two anaerobic isolates were identified- *Veillonella parvula* and *Bacteriodes bivius*. There were 11 mixed aerobic infections, with only one mixed aerobic/

anaerobic infection involving *Veillonella sp.* and *Haemophilus sp.* Other isolates included *Streptococcus viridans*, Group A streptococcus, *Staphylococcus epidermidis* and *hyicus*, and a hemolytic streptococcus not otherwise specified. The distribution of organisms identified can be found in Table 1.

## DISCUSSION

Our results concur with earlier findings: *S. pneumoniae* and *H. influenzae* were the most common isolates in this series of pediatric chronic infections, as cited by Feigin and Cherry.<sup>6</sup> Although anaerobes appear to play some role, our study does not substantiate the prevalence noted previously by Brook.<sup>3</sup>

As with prior work in this area, our data is somewhat limited due to study group size. In addition, bacterial colony counts and cytopathology would insure that cultures reflect actual sinus infection rather than colonization or contamination. The significance of our results, how-

ever, underscores the need for continued investigation in this area with a larger cohort and modified culture technique.

Children with recurrent or persistent sinusitis should be evaluated thoroughly, including radiological study, to identify any underlying congenital or acquired abnormality.<sup>15</sup> Antimicrobial therapy should be instituted and directed at common pathogens. Pneumococci are almost always sensitive to penicillin, but *H. influenzae* and *M. catarrhalis* are often beta-lactamase-producing. Therefore, amoxicillin and potassium clavulanate, erythromycin and sulfisoxazole, or cefaclor, should provide appropriate antimicrobial coverage for offending organisms. However, the efficacy of antibiotic therapy at this progressive stage of disease is itself in question. The chronically inflamed sinus membrane with decreased vascularity may be a poor transport medium for attaining adequate tissue level antibiotics in spite of therapeutic blood levels. A reduction in

Table 1

AEROBES			
Organism Identified	# of Isolates Identified	Proportion	Confidence Intervals (95%)
<i>Haemophilus influenzae</i>	7	.28	.10 - .46
<i>Streptococcus pneumoniae</i>	7	.28	.10 - .46
<i>Staphylococcus aureus</i>	6	.24	.07 - .41
<i>Moraxella catarrhalis</i>	5	.20	.04 - .36
<i>Streptococcus viridans</i>	4	.16	.02 - .30
Group A Streptococcus	1	.04	.04 - .12
Hemolytic streptococcus-NOS	1	.04	.04 - .12
<i>Staphylococcus epidermidis</i>	1	.04	.04 - .12
<i>Staphylococcus hyicus</i>	1	.04	.04 - .12
ANAEROBES			
Organism Identified	# of Isolates Identified	Proportion	Confidence Intervals (95%)
<i>Veillonella parvula</i>	1	.04	.04 - .12
<i>Bacterioides bivius</i>	1	.04	.04 - .12



oxygen tension and pH may interfere with antimicrobial activity as well, even in the presence of appropriate serum concentrations.

Decongestants theoretically should aid in reestablishing the patency of the natural sinus ostia. In fact, the use of a topical pediatric nasal decongestant for a period of three to five days may promote drainage and aeration of the sinuses. Some sources, however, feel systemic preparations impair delivery and diffusion of antimicrobials into the tissues. The use of antihistamines is also debatable. Some researchers feel they produce ciliostasis and may delay clearance of infected material. The exception to their use is in the allergic child who may also benefit from the addition of cromolyn sodium, a mast cell stabilizer, and a topical steroid spray to reduce mucosal edema. When medical management fails, however, surgical consultation is in order.

The introduction of pediatric functional endoscopic sinus surgery (FESS) in the 1980's revolutionized the surgical approach to sinusitis in children. FESS is a functional rather than an ablative or exenterative procedure. In addressing problems of the osteomeatal complex, pathological tissues are removed and normal tissues are left in place. FESS corrects anatomic obstructions and reestablishes conditions that enhance normal mucociliary clearance.

FESS should be considered for all patients who fail to respond to repeated, prolonged trials of medical therapy.<sup>12</sup> Overall, management of chronic sinusitis in children remains open to research. For now, prudent judgment warrants antimicrobial therapy aimed at common patho-

gens in conjunction with surgical consultation. □

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# Address of the President

William C. Gates, Jr., MD

*Presented to the MSMA House of Delegates, Thursday, April 29, 1993, in Biloxi, Mississippi.*

**I**t seems like only yesterday that we were embarking on a brand new association year, only to wake up this morning and find out that it's over already.

I've been told that when you get older the days and nights get much longer and the years get much shorter — well, I guess I'm there — this year has gone by at "warp" speed.

Another sign of getting older is when you have trouble getting your rocker started. I've noticed that, too. L. L. my lovely wife and wonderful partner, has made some observations in this regard also — probably not what you're thinking — anyway, she tells the story that one afternoon when she handed me my sweater, I looked up and asked her as I was taking it, "Am I cold or are we going somewhere?"

I may be feeble, but I'm looking forward to a great meeting and having fun as well as a wonderful educational experience here in beautiful Biloxi.

We are indeed fortunate to have our dedicated and hard-working AMA Speaker of the House, Stormy Johnson, visit

with us and share his view of where we find ourselves as members of organized medicine in this age of angst. We are pleased and proud to have you here with us, Dr. Johnson. Thank you sin-



*Dr. William C. Gates, Jr.*

cerely for coming and sharing your insight with us.

Before I go any farther, let me thank this House of Delegates, from the bottom of my heart for the opportunity, the challenge and the privilege of serving as

your president.

This has been the greatest honor of my professional life and I shall cherish the memory of this year forever. L. L. and I have truly enjoyed traveling the length and breadth of the state and getting to visit with the various component society members and their spouses. We appreciate the warmth and hospitality we experienced everywhere we went.

I also want to take a moment to give some indication of my profound appreciation of our staff. I have had occasion over the last 20-25 years to observe staff in most of the other states and I'm here to tell you that I would put ours up against anybody else's, anywhere, anytime! Thank you — Charlie, Bill, Clare, Robert, Kay, Barbara, Ginger, Jackye, Patsy, Barbara and Lora — again, thank you deeply for all that you do! Words don't adequately express my feelings in this regard.

This sounds like a whole lot of thanking going on, but I must thank my family for their understanding and their support, particularly my wife L. L. who, in

spite of her very busy profession and many, many service activities at local, state and national levels, found the time to go with me to all the meetings except one — she's a pretty good copilot, too. She was also kind enough to share her views as a state Auxiliary vice-president for legislation.

There is no way to satisfactorily thank my two partners, Bob Howland and Ed Morrison, for all their sacrifices to allow me a flexible schedule, but I will continue to try to repay them for their indulgence.

The same goes for my wonderful office staff at home — Ann, Faye, Mickey, Kathy, Peggy, Roxann, Brenda, Tanya, Jeannie and Debby — so supportive in so many ways and often on such short notice. Thanks, Gang!

Now, I want to thank God for allowing me to be one of those lucky people who get to live in this wonderful country of ours with all its benefits and freedoms — America — the U.S.A.

With all its shortcomings, it's still the best place in the world to live and work. Our political system, after acknowledging its rough spots, is still the finest around. Even though we are sometimes reluctant to admit it, the system is the greatest and most representative form of government on the planet. We as physicians just haven't learned to properly participate in the process, and we have a vast, untapped power base that is a sleeping giant because of the lack of involvement and understanding. I hope to live long enough to see that giant wake. Too many of us consider ourselves "above politics" and that serves as an anesthetic for the giant.

We have the finest health care

in the world — notice I said "healthcare" — not "health care system." The delivery system is in bad need of not just repair, but overhaul.

Unfortunately, the polls are showing that the general public perceives the problem to be that "The doctors make too much money." Included along with the doctors, are insurance companies, hospitals, drug companies and lawyers, but we doctors are the lightning rods for this issue.

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**'I fear that the political ploy developing here, to use a western movie metaphor, is to paint the physicians as the bad guys in black hats riding black horses — and in rides ole hopalong Clinton, wearing the white hat and riding the white horse, to rescue the damsel in distress, i.e., the general public, from the bad guys.'**

---

If that ploy is successful, it would place political capital in votes for the health system reform package yet to be announced by the Clinton administration, but probably containing some elements of fee-freezing, price controls, managed competition and global budgets, all concepts that are somewhat onerous to organized medicine.

It would serve us well to remember that old saying, "Those who ignore history are doomed to repeat it."

History has shown that fee-freezes and price controls have never worked in 4,000 years and that they always bring harmful effects. This has been true since the time of the Hammurabi Code.

Managed competition is still

theoretical and untried, still a gleam in the economist's eye and may be an oxymoron, like "The Bush Campaign" or "Airline Cuisine".

Global budgets, according to most experts, will surely lead to further rationing of care. Alain Enthoven, an economist from Stanford, describes global budgets as being "like bombing from 35,000 feet - you don't have to see the faces of the people you are killing." That's a pretty graphic and accurate explanation, in my opinion.

As to why organized medicine hasn't been consulted more regarding the system reform, Rep. Phil Gramm of Gramm-Rudman-Hollins fame said the following at the recent meeting we attended in Washington.

It's hard to write visionary plans when you have to deal with people who actually know something about the problem.

I derived some comfort at that meeting from hearing a couple of socialized medicine die-hards, Pete Stark and Ted Kennedy, talking in terms of physician autonomy, patient choice, reduction of hassle factors and tort reform, more in line with the conservative democratic forum than the radicalism of the past, I thought.

Senator Kennedy told a story on himself worth passing on, he recounted speaking to a large group of people out west and a heckler stood up in the back of the room and yelled, "Kennedy is a horse's ass," whereupon the heckler was very quickly and forcefully ejected. Kennedy then remarked to the audience that he didn't realize he was in Kennedy country and the master of ceremonies stood and said, "you are not in Kennedy country, Senator, but this is horse country."

I had occasion to hear Senator Rockefeller speak at a lead-



ership conference in Atlanta the month before the Washington meeting where he also spoke and I was struck by his opening statement which was "The fact that there are so many more people here than anticipated was totally predictable."

I use that as a demonstration of the fact that our Congressmen do occasionally lapse into oxymoronic circumlocution.

I am spending a fair amount of time talking about health system reform, because I think it is the number one issue of these interesting times. I don't think that we will go to sleep one night and wake up the next day with a new system — I believe there is time and a window of opportunity to influence the rate and nature of the change **if we get united, get inspired, get inventive and get involved** in pushing for reform that centers around the tenets of *Health Access America*, but ready to be flexible and compromise where needed and appropriate.

Victor Fuchs, another economist at Stanford, had an article in the April, 93, *JAMA* and I was impressed with his uncharacteristically accurate observations. Economists, you know, are the ones who predicted 7 of the last 2 recessions. Uwe Reinhardt, a Princeton economist and member of the PPRC said that an economist is a guy who can describe a thousand ways to make love, but doesn't know any girls. Back to Mr. Fuchs. He asks that President Clinton give Congress and the public a clear statement of, and rationale for, his goals for health care and his basic approach to achieving those goals. A true statesman would do just that. President Clinton, however, has chosen to be politically sinister.

Mr. Fuchs reminds us that

most Americans believe that the large profits of drug companies and excessive physician incomes are the main problems. They are not.

If drug company profits were slashed in half, health care costs would fall by less than 1%. If physicians' net incomes were cut by 20%, health care costs would fall less than 2%.

Mr. Fuchs admonishes the President to provide leadership for a major effort to educate the public about the *real* problems in health care.

He identifies three changes absolutely necessary to avoid catastrophic collapse of the system within a decade:

First, he feels we must disengage health insurance from employment - there must be subsidization of those unable to afford insurance and compulsion for those who are unwilling to acquire it. He feels that link between employment and insurance is an artificial one. This is a departure from the employer mandate found in *Health Access America*.

Second, we must tame but not destroy technologic changes in medicine. Technologic change is the most important force behind the escalation of health care expenditures. There is too much of it and some of it is misdirected. It is strange, but true, that society is willing to pay heavily for any innovation that offers even a small promise of postponing death, yet the healthy population is not as willing to pay for the preventive innovations that would save many more lives for each dollar of expenditure.

Third, we must learn to cope with an aging society. The elderly consume 40% of all health care in the U.S. and the percent will continue to grow. No nation can afford a health policy that

provides the elderly with *all* the care that *might* do them *some* good *without regard to costs*. A large percentage of that expenditure is in the last six months of life.

Success in dealing with these three central issues will require major improvements in our governmental institutions. The market is a powerful and flexible instrument for allocating most goods and services, but it cannot create an equitable, universal system of insurance, cannot harness technologic change in medicine and cannot cope with the potentially unlimited demand for health care by the elderly.

On the other hand, the savings and loan debacle, the HUD scandals and the cost overruns in defense procurement do not inspire confidence that our government can currently handle the complex issues of health care efficiently and honestly. Thus, major political reform in general and in the health area in particular, is a necessary precondition for significant improvements in the health care system.

---

**'The biggest challenge for President Clinton is to lead that political reform and educate the public as to what the real problems are.'**

---

Mr. Fuchs is on target, for the most part, and I think shares that certain vision of purely governmental health care as a system characterized by the *efficiency* of the postal service, the *cost containment* of the Pentagon and the *compassion* of the IRS.

I believe that common sense and practicality will eventually rule that day after an enormous debate and that there is a great

potential for good to come out of this unbelievably complex problem. All we have to do is provide access to quality affordable care to about 250 million people.

Can we do it? Of course we can — but it will be predicated on a partnership with common purpose for all the panoply of players participating in the reform program.

Can we influence the nature of the change? I believe so — as long as our debate is on the high road, steeped in patient advocacy and promoting policies that protect professionalism and the dignity of the practice of medicine.

Having said all that, let's switch topics now and talk some about the association.

The association has had a good year - we are fiscally sound, our service programs are in good shape, we had a pretty good legislative year and membership is reasonably stable.

The membership survey has revealed some areas that need attention and you will hear more about that in some of the board reports. Your MSMA staff, the Board and the Councils have performed in a dedicated, diligent and dutiful manner to accomplish your objectives prudently and judiciously. We are indeed fortunate to have excellent leadership for the coming year when Dr. Don Q. Mitchell takes the helm.

The Auxiliary has had a great year with the capable leadership of Kathy Carmichael and her talented and enthusiastic officers and will have another great year with Peggy Crawford's direction. The catch phrase for their leadership conference has haunted me - It was: *No one of us is as smart as all of us*. I have enjoyed working with the Auxiliary throughout the year.

Our AMA delegation has had

a flurry of positive activity, also. Sidney Graves has served as Chair of the Southeastern Delegation, Ed Hill is on the Council on Legislation, George McGee is on the Council on Long Range Planning and Faser Triplett is a candidate for the AMA Board of Trustees after serving as Chair of AMPAC. Carl Evers, prior to his untimely death, was on the Council on Medical Education. Jimmy Waites is serving at the national level on the Medicare Advisory Board. Candace Keller is serving on the Women in Medicine National Advisory Board. Lamar Weems serves on the Executive Committee of the American Urological Association and I serve as Southeastern Representative to the Board of Directors of the American Association of Clinical Urologists. We have an active, busy delegation.

I'm sure there are several other members of the association who serve in national offices for specialty societies - I'm sorry I can't name you all. I would like to recognize the fact that Richard Hollis from Amory is serving as National President of the American College of Obstetrics and Gynecology.

My recommendations as I leave you as president are several and simple.

**First:** We have a number of excellent programs in place that need emphasis and focus. I'm thinking particularly about *Health Access Mississippi* and the *Comprehensive Health Education Curriculum*. "Health Choice", a wonderful program jointly sponsored by the association and the Auxiliary, should be expanded to at least 3 sites in the state and advertised and celebrated. The Auxiliary is a magnificent resource for our association and serves us well as medi-

cal ambassadors. The public relations value of the "Health Choice program" is immeasurable.

**Second:** I think we should broaden the format for the President's visit to the component societies. We need to hear from the Auxiliary. It is also invaluable and instructive to hear about local legislators and legislation. I hope Clare Hester will continue to agree to do that for us. All this to be done with the objective of spreading knowledge, not just information, to the association's members.

**Third:** We should encourage and support the Council of MSMA Past Presidents, suggested by Jimmy Waites last year to study the issue of cost and access to quality health care. We will have a report from that Council at this meeting. I hope that this Council, with its vision, experience and dedication, will accept other toothy issues over time, and serve as a tremendous resource for the exploration and elucidation of those kinds of problems.

**Fourth:** I would like to see the continuation and augmentation of the trend in our association to be in the **knowledge** business, not just the information business. Our members need to know not just **what** decisions were made but **why** those decisions were made. We need to know the impact on us personally and professionally of the information we receive. Information is power but not as **powerful or as empowering as knowledge**. This interfaces with Recommendation No. 2.

**Fifth:** We should be able, by using good two-way communication, to define for the membership a clear vision of an achievable future. Unity of mind and purpose is the reason for ac-



ceptance by the membership of a clear, common, concise and shared vision with reachable goals.

**Sixth:** I would like to urge a renewed, vigorous commitment to our profession and our association. There is now a **real** need to be **cohesive, coherent and committed**. The individual physician in this new world of change has never had a greater impetus to **get informed, get in-**

**vested and get involved** in influencing his personal and professional future. There should be no question as to where membership stops - It's from the grassroots to the top of the federation. Remember the old Indian adage, "The strength of the **pack** is the **wolf**, and the strength of the **wolf** is the **pack**."

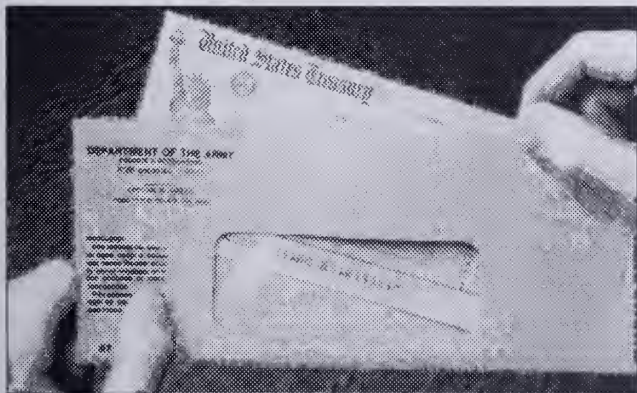
I will close now with another sincere and heartfelt thank you for allowing me the honor and

privilege to serve you. My wish for each of you is for you to achieve the personal and professional fulfillment you desire and deserve in an environment that promotes and preserves patient advocacy, the dignity of the practice of medicine and the sanctity of the Doctor-Patient Relationship.

Thank you. □

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## **The President's Page**

**DON Q. MITCHELL, MD**

### **A Level Playing Field**

**T**oo often when discussing health care costs, the finger is pointed at the physician. As Bill Gates said in his recent presidential address, "we doctors are the lightning rods for this issue". If the health care reform game is to be played fairly, then it needs to be played on a level field.

It is my opinion that it is our (the physician's) obligation to educate our patients about health care costs. We have the opportunity to talk to them face to face, one on one, about this issue.

Of the \$820.7 billion total cost of U.S. health care in 1992, spending for physician services accounts for only 19%. This includes overhead expenses, such as professional liability insurance, salaries of professional and clerical staff, rent, office supplies, and equipment. Since physician income makes up such a small portion of total U.S. health expenditures, what are some of the things included in the other 81%?

Our patients need to know that much, though certainly not all, of the impetus behind the growth in health care expenditures can be traced to life-style factors and social problems. Smoking-related illnesses accounted for nearly one in five deaths in 1990 and cost the government \$68 billion, or \$1,078 per smoker, according to Congress' Office of Technology Assessment. Smoking-related diseases killed 417,000 Americans in 1990. Alcohol is an equally dangerous health threat. The unwise consumption of beer, wine and liquor results in 100,000 deaths and at least \$100 billion in economic costs annually. Drug abuse adds more than \$60 billion in costs to the health care system and violence adds more than \$6 billion. These life-styles and forms of social behavior can be changed.

The aging of the U.S. population is also a factor in rising health care spending. Our patients need to understand that with the best health care system in the world utilizing the latest technical advances, most people will live longer. With this

*(Continued on page 194)*



## Overall Physician Cost Effectiveness

In this era of managed care, the cost effectiveness of individual physicians is being studied in detail by many entities, including government, insurance companies, hospitals, and consumer groups. Data to reflect this cost effectiveness are being gathered, analyzed, and utilized to select "cost effective" physicians for various managed care entities. Unfortunately, most of these data are based on hospital-based care, and do not pay due respect to OVERALL physician cost effectiveness. What are the indicators of true physician cost effectiveness? The following factors, although not necessarily exclusive, should certainly be included:

1. Physician charges.
2. Physician prescribing habits and the costs generated.
3. Accuracy of diagnosis and appropriateness of treatment.
4. Propensity to admit to the hospital as opposed to maximum use of outpatient care.
5. Appropriateness and volume of follow-up services.
6. Appropriateness and timeliness of ordering

ancillary studies (lab, x-ray, etc.) in evaluation and treatment.

7. Length of stay of hospital patients, which may reflect not only the critical path scheduling ability of the physician, but also the efficiency of the hospital services.

It appears that the determination of overall physician cost effectiveness is quite complex, and a degree of sophistication will be required to evaluate and apply this entity both accurately and fairly. However, because physicians may be discriminated against based on this determination, and because that discrimination will affect the livelihood of those physicians deemed not cost effective, it is imperative that ACCURACY and FAIRNESS are preserved in the utilization of the concept of cost effectiveness. Just as important, the use of OVERALL cost effectiveness is the only way that optimal use of health care resources can be achieved (which is the goal of using "cost-effective" physicians in the first place).

**George E. Abraham, II, MD**  
Associate Editor

The editorial opinions expressed in this Journal are those of the indicated author. Editorial opinions are not expressions of the views, or official policies of The Mississippi State Medical Association. We encourage the membership to submit letters for publication regarding any opinion expressed or information contained in the Journal.

## President's Page

(Continued from page 192)

progress comes an increase in health care costs. Per-capita health costs for those under 65 years of age is approximately 72% of the national average while per-capita costs for those 85 and over is 750% of the national average.

Finally, our patients need to realize the cost of this litigious society. In 1989, the total professional liability cost relating to physician services was \$20.7 billion, of which \$15.1 billion

was attributable to physicians defensive medical practices.

Much has been written, discussed and debated about the right of every American to have access to adequate health care services. Less has been publicized about the responsibilities that come with that right. The report of the AMA Council on Ethical and Judicial Affairs, which will be presented at the June meeting, states it this way, "Patients should be committed to health maintenance through health-enhancing behavior. Illness can often be prevented by

a healthy life-style, and patients must take personal responsibility when they are able to avert the development of disease."

Patients could be our greatest allies. They need to have these health issues explained to them and unless we do so, it virtually guarantees that we will continue to play this game on an unlevel playing field.

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## Physicians Invited to Discuss Administration's Reform Plan

J. Edward Hill, MD, of Hollandale, was one of ten practicing physicians who met with Mr. Ira Magaziner, on Tuesday, May 25, in Washington, D. C. for a three and a half hour session to discuss the Clinton Administration's Plan for health care reform. Mr. Magaziner is coordinator of the Clinton Health Care Reform Task Force.

The purpose of the meeting was to get the individual physician's input about the plan before it is actually sent to Congress, which according to the information presented at the meeting will be before the 4th of July.

Dr. Hill was the only family physician present representing a rural southern state, and a state which does not currently have state legislation enacted or proposed for health reform.

Although the actual plan document was not presented for review, Mr. Magaziner gave an outline of each item in the plan. Dr. Hill and the other physicians were asked to respond and make suggestions.

Dr. Hill said, "I feel much more comfortable about the task force and the reform process. Mr. Magaziner was very knowledgeable about the issues and seemed sincere in his desire to improve the health care system. I was especially pleased with his concern

for rural states like Mississippi and the issues we face."

Some of the key points currently in the plan and discussed at the meeting were:

1. Universal access to care - with an employer/employee mandate phased in over a 5 to 7 year period.

2. A comprehensive basic benefit package - including prescription drugs and mental health benefits - to be offered through several delivery methods such as health maintenance organizations (HMOs) or physician provider organizations (PPOs). Additional coverage above the basic package could also be purchased.

3. Insurance reform to include community rating, non-exclusion for pre-existing conditions, and portability of coverage. Every person would be issued a Health Security Card.

4. Access to care in rural areas would be addressed through "managed collaboration" - the establishment of networks within a geographic region to provide health care. "A key issue of concern in this area continues to be the availability of primary care physicians in rural areas," Dr. Hill said, "and Mr. Magaziner discussed several incentives being considered to encourage physicians to practice in rural areas to include increased reimbursement to physicians providing care in rural areas, medical loan forgiveness, funds available for recruitment, and possible changes to the current National Health Service Corp."

Professional liability reform was also discussed. Dr. Hill said, "Mr. Magaziner reported that the reform plan was looking strongly at 'Enterprise Liability' and as a group we disagreed with this". Enterprise Liability would mean that a managed care organization would be the responsible party for liability not the individual physician. "I think he (Mr. Magaziner) was surprised by our reaction. We think the individual physician needs to be responsible for his actions. However, what we do need is a limit or cap on the amounts paid in professional liability cases. We suggested that they look at California's MICRA laws (Medical Insurance Compensation Reform Act). These laws are in place and are working. The 'Enterprise Liability' plan is a new idea and has never been tried."

Regulatory relief is of key concern for all physicians and these areas are also addressed in the administration's plan. The current requirements under the Clinical Laboratory Improve Act (CLIA) would be significantly altered such that physician office laboratories would not be included in the inspection process and the compliance features would be much simpler. Also Medicaid and Medicare changes would not be issued more than once or twice a year and a single form would be used for all claims. Mr. Magaziner further reported that plans are to do away with the yearly "Attestation Statement" required by Medic-

aid. Additionally, the ERISA exemptions will continue and he emphasized several times that the administration was not going to micro-manage physicians or hospitals.

"The idea of managed competition is very much alive," Dr. Hill

said, and at one point Mr. Magaziner stated, "physicians must take charge of the system. They must organize themselves as never before. The onus is on physicians to develop and provide networks for care."

Dr. Hill noted that, "Two specific times during our meeting we asked Mr. Magaziner about the cost involved in this plan and he gave us no answer either time. He did

say however that they wanted to wait until after budget reconciliation before cost was discussed."

Many other issues were discussed during this meeting and the group of ten physicians will be invited back to Washington to meet with Mr. Magaziner in order to review the final plan document before it is presented to Congress.

□



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## 125th Annual Session Highlights



▲ During the Sunday MSMA House of Delegates Session, *Don Q. Mitchell, MD of Jackson, center, was installed as 1993-94 MSMA President. Mal G. Morgan, MD of Natchez, left, was named president-elect. William C. Gates, Jr., MD, right, is immediate past president of the Association.*

### **Dr. Mitchell Installed as President; Dr. Morgan Named President-Elect**

Dr. Don Q. Mitchell of Jackson was installed as 1993-94 president of the MSMA and Dr. Mal G. Morgan of Natchez was named president-elect during the closing session of the House of Delegates on Sunday, May 2, 1993.

Dr. Mitchell was also elected to serve as a delegate to American Medical Association.

Prior to his year as president-elect, Dr. Mitchell served the MSMA as secretary-treasurer for two consecutive terms (1986-1992).

Dr. Mitchell is in practice at the Mississippi Asthma and Allergy Clinic, PA and is board certified in both allergy and immunology. He is a member of numerous medical organizations including the American College of Allergy and Immunology, the American Association of Certified Allergists, the American College of Physicians, and the

American Academy of Allergy and Immunology. He is a member of the Board of the MSMA Benefit Plan & Trust and recently served as vice-chairman of the Mississippi Comprehensive Health Insurance Risk Pool Association.

Dr. Morgan is an internist, practicing in Natchez. He has served the association as chairman and vice-chairman of the MSMA Board of Trustees and as an alternate delegate to the AMA. □



# Elected Officer, Board and Council Members

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**Mal G. Morgan, MD** of Natchez

## SPEAKER OF THE HOUSE

**H. Vann Craig, MD**, Natchez

## VICE-SPEAKER OF THE HOUSE

**George E. McGee, MD**, Hattiesburg

## DELEGATE TO AMA

**Don Q. Mitchell, MD**, Jackson

**J. Edward Hill, MD**, Hollandale

**James C. Waites, MD**, Laurel

## ALTERNATE DELEGATE TO AMA

**George E. McGee, MD**, Hattiesburg

**Candace Keller, MD**, Hattiesburg

**W. Lamar Weems, MD**, Jackson

## ASSOCIATE EDITOR, JOURNAL MSMA

**Leslie E. England, MD**, Natchez

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**Robert S. Rhodes, MD**, Jackson



▲ Members of Central Medical Society joined Dr. Mitchell, at the podium, as he was given the oath of office by Dr. Morgan, chairman of the Board of Trustees. Mary Sue Mitchell held the Bible as the oath was given.



▲ Dr. William C. Gates, Jr. of Columbus was presented his past president's pin by Dr. Don Mitchell.



▲ Mrs. Peggy Crawford, left, wife of Dr. Dewitt Crawford of Louisville, was installed as president of the MSMA Auxiliary. She is pictured with MSMA President Dr. Don Mitchell.

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## Actions of the House of Delegates

### 125th Annual Session April 28 - May 2, 1993

MSMA's House of Delegates acted on a broad range of reports from the Board of Trustees and MSMA's Councils, as well as resolutions. Some of the significant actions taken by the House are:

- Directed that a MS Physicians' Service Network be established by the association within the context of health system reform efforts to address access, quality and cost issues.
- Went on record to support legislation requiring a beneficiary co-payment for home health services and an explanation of medical benefits (EOMB) when such services are rendered.
- Directed that the advice and support of the AARP be sought for legislation requiring periodic recertification of motor vehicle operators over age 70.
- Directed the Board of Trustees to study the advisability of raising the minimum age for a drivers license in Mississippi to age 16.
- Directed the Board of Trustees to take necessary action to obtain a fair and equitable physicians' fee schedule for the MS Workers' Compensation program.
- Endorsed the National Vaccine Advisory Commission's Standards for Immunization Practice and urged all physicians to promote immunizations and actually participate in community-based efforts to fully immunize at least 90% of all children under age
- Presented the MSMA Community Service Award to Dr. Antone W. Tannehill, Jr. of Tupelo.
- Presented special appreciation awards to Drs. Ellis M. Moffitt and Nina Goss-Moffitt of Jackson for their work in establishing and conducting the MSMA Impaired Physicians Program.
- Directed the Council on Medical Service to study and recommend the need for a medical home for indigent children.
- Directed that a study be made of the health needs of the incarcerated.
- Adopted a new process for nominating members to serve in elected offices of the association, whereby nominations will be solicited from the general membership and the nine immediate past presidents of the association will serve as a nominating committee.
- Voted to continue alternating Annual Sessions of the asso-

ciation between Jackson and the Gulf Coast and to investigate other sites within the state when such sites become available with adequate space to accommodate Annual Sessions of the association. □

#### Members Serving on Reference Committees of the House were:

##### *Reference Committee on Rules and Order of Business*

Ralph L. Brock, MD, Chairman  
W. Joseph Burnett, MD

##### *Reports of Officers, Board of Trustees and Councils*

##### *Reference Committee A*

Leslie E. England, MD, Chairman  
Karl W. Hatten, MD  
Dwalia S. South, MD  
S. Jay McDuffey, MD

##### *Reference Committee B*

Mickey P. Wallace, MD  
C. Foster Lowe, MD  
Mary Gayle Armstrong, MD  
Candace E. Keller, MD

##### *Reference Committee on Credentials*

D. Stanley Hartness, MD  
John H. Cook, MD

##### *Reference Committee on Constitution and Bylaws*

Chester W. Masterson, MD, Chairman  
Ben W. Carmichael, MD

##### *Nominating Committee*

John J. Cook, MD, Chairman  
Edwin M. Hemness, MD  
Stanley Hartness, MD  
Mary S. Gaines, MD  
John C. Clay, MD  
Thad F. Waites, MD  
Chester C. Masterson, MD  
Roy D. Duncan, MD





▲ *Chester Masterson, MD, Vicksburg, Chairman Reference Committee on Constitution and Bylaws*



▲ *Lee England, MD, Natchez, Chairman Reference Committee A*



▲ *Mickey Wallace, MD, Jackson, Chairman Reference Committee B*



▲ *MSMA Delegates and members had the opportunity to participate in all reference committee meetings.*

*Reference Committee A was held, Thursday, April 29.*

*The Reference Committee on Constitution and Bylaws and Reference Committee B were held on Friday, April 30.*

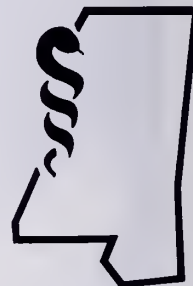
◀ *John Patterson, MD of Pontotoc, left and ▶ Lee Rogers, MD of Tupelo, right, spoke to issues before the reference committees.*





◀ Kirk Mullins, of Natchez, left, was the recipient of The Carl Gustav Evers Award. William C. Gates, Jr., MD, right, presented this first award with Mrs. Jan Evers, center.

*The Carl Gustav Evers Award will be given annually by the Mississippi State Medical Association Foundation on behalf of the many friends and colleagues of Dr. Carl Evers, a past president of the association, member of the AMA Council on Medical Education and associate dean of academic affairs in the School of Medicine and presented to the senior medical student who has demonstrated qualities of peer to peer support, scholarship and exceptional leadership in promoting and participating in student activities of The American Medical Association and The Mississippi State Medical Association.*



▲ Antone W. Tannehill, Jr., MD, left, of Tupelo was presented the 1993 MSMA Community Service Award by William C. Gates, Jr., MD, president.

► Karen Abernathy, health reporter, WLOX-TV was presented the 1993 Award For Excellence In Medical Reporting by Mickey P. Wallace, MD, chairman of the Council on Public Information.





► An award of special appreciation was presented to Drs. Ellis and Nina Moffitt for their unselfish, unconditional and continuous efforts to improve the lives of others through the MSMA Physicians Recovery Program and the Caduces Club.

The award was accepted by their children, Dr. Ginny Moffitt Crawford of Hattiesburg and Dr. John Moffitt of Jackson.



◄ Van L. Lackey, MD, left, accepted the Aesculapius Award in the Scientific Exhibit section. The exhibit entitled **Growth Factors** was submitted by Jackson Oncology Associates - Mack C. Furr, MD; Guy T. Gillespie, Jr., MD; Bobby L. Graham, Jr., MD; Gerry Ann Houston, MD; Van L. Lackey, MD; and G. C. Stubblefield, MD. The award was presented by Stanley Hartness, MD, Secretary/treasurer of Association.



► Dewitt Crawford, MD, of Louisville, right, won the Technical Exhibit Attendance Prize. The award was presented by Stanley Hartness, MD.



▲ *Dave Duddleston, MD, served as Chairman of the Medicine Plenary Session.*



▲ *Medicine Plenary Session*



▲ *Robert Rhodes, MD, served as Chairman of the Surgery Plenary Session.*



▲ *Surgery Plenary Session*



▲ *Dewey Lane, MD, spoke to the Hospital Medical Staff and Young Physicians Section meeting.*



▲ *John Patchett, JD, from AMA spoke to both the Medicine and Surgery Plenary Session.*



▲ *Howard Waltman, SANUS Corporation Health Systems spoke during the Medicine Plenary Session.*





◀ *The Doctors Four Musical Quartet from Laurel presented special music for the Sunday morning service.*

*They are, from left, David Rice, DDS; John Hassell, MD; John McGraw, MD; and Eric Lindstrom, MD.*

*Dr. McGraw, president of the Baptist-Medical Dental Fellowship delivered a message on the "Call to Physical Healing".*



◀ *Delegates vote on new officers and council members during the Sunday Session of the MSMA House.*



▲ *Vann Craig, MD, left, is Speaker of the House and Eric McVey, MD, right, is Vice-speaker.*



▲ *Leonard H. Brandon, MD of Starkville speaks to a reference committee report during the closing session.*



◀ **MSMA Auxiliary President Kathy Carmichael, wife of Ben Carmichael, MD, from Hattiesburg addresses the opening session of the MSMA House of Delegates.**



► **MSMA Auxiliary Officers: seated from left, Peggy Sprabery, third vice-president (AMA-ERF) Pass Christian; Jeanne Morrison, second vice-president (health promotions) Hattiesburg; Peggy Crawford, president, Louisville; Barbara Webb, recording secretary, Jackson; Nancy Bush, first vice-president (membership) Laurel; and Nell Middleton, fourth vice-president (legislation) Winona; and standing, Jo Waites, parliamentarian, Laurel; Jane Ladner, treasurer, Jackson; Karen Stephens, president-elect, Hattiesburg and Kathy Carmichael, immediate past president, Hattiesburg.**



◀ **MSMA Auxiliary Past Presidents met for breakfast on Saturday morning during the annual session. Seated from left, Sylvia Walker, Jackson; Peggy Crawford (incoming president), Louisville; Kathy Carmichael, Hattiesburg, and Martha Tatum, Hattiesburg.**

**Standing from left, Merrell Rogers, Tupelo; Jean Hill, Hollandale; Roberta Barnett, Brookhaven; Nancy Lindstrom, Laurel; Peggy Herrington, Natchez; Martha Clippinger, Gulfport; and Jo Waites, Laurel.**



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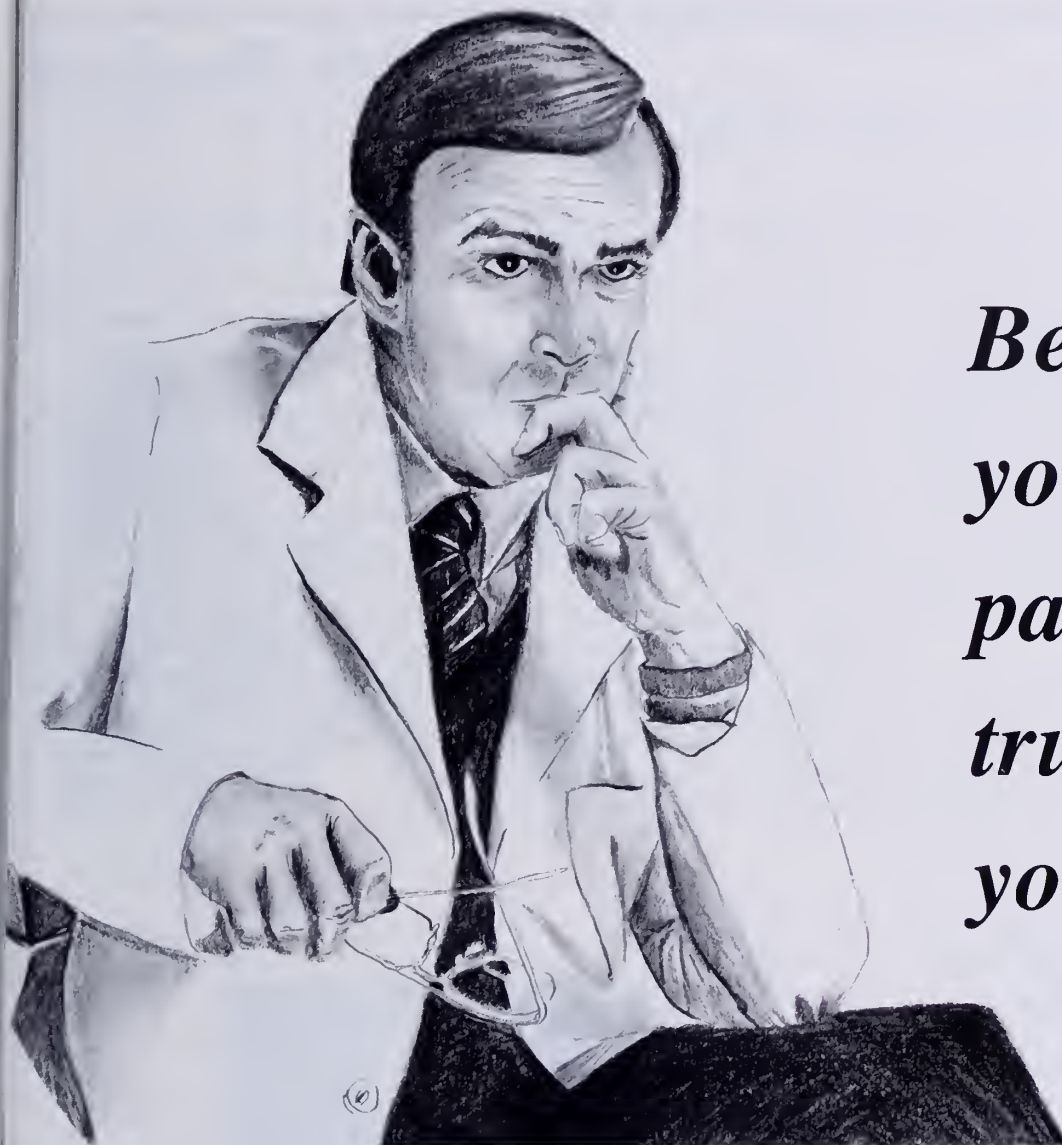
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## New Members

**Davis, Ronald D.**, Jackson. Born Shaw, MS, August 28, 1959; MD, Medical College of Wisconsin, Milwaukee, WI, 1985; interned one year and two year surgery residency, Columbus Hospital, Chicago, IL; general surgery & urology residency, University Medical Center, Jackson, MS, 1987-92; elected by Delta Medical Society.

**Derbes, Lawrence J., Jr.**, Hattiesburg. Born Baton Rouge, LA, July 30, 1959; MD, Louisiana State University School of Medicine, New Orleans, LA, 1985; interned and medicine residency University of South Florida College of Medicine, Tampa, FL, 1985-88; cardiology fellowship, University of California School of Medicine, Davis, CA, 1988-90; elected by South Mississippi Medical Society.

**Flanagan, Karen Ann**, Natchez. Born Gardiner, ME, January 1, 1954; DO, Kirksville College of Osteopathic Medicine, Kirksville, KS, 1980; one year internship Cuyahoga Falls General Hospital, Cuyahoga Falls, OH; elected by Homochitto Valley Medical Society.

**Friloux, Mark A.**, Columbus. Born Killern, TX, January 25, 1958; MD, University of Mississippi School of Medicine, Jackson, MS, 1984; interned and medicine residency Baptist Memorial Hospital, Memphis, TN, 1984-87; elected by Prairie Medical Society.

**Gilliland, David H.**, Tupelo. Born Kosciusko, MS, July 28, 1958; MD, University of Mississippi School of Medicine, Jackson, MS, 1987; interned and general surgery residency, University of Louisville School of Medicine, Lexington, KY, 1987-92; elected by Northeast Medical Society.

**Lenox, Valerie R.**, Biloxi. Born Washington, DC, July 10, 1960; MD, Louisiana State University School of Medicine, New Orleans, LA, 1987; medicine residency, University Medical Cen-

ter, Jackson, MS, 1987-90; elected by Coast Counties Medical Society.

**Moman, Maria M.**, Gulfport. Born McComb, MS, September 13, 1943; MD, Howard University College of Medicine, Washington, DC, 1974; interned one year Freedman's Hospital, Washington, DC; ob-gyn residency, Howard University Medical Center, Washington, DC, 1975-79; elected by Coast Counties Medical Society.



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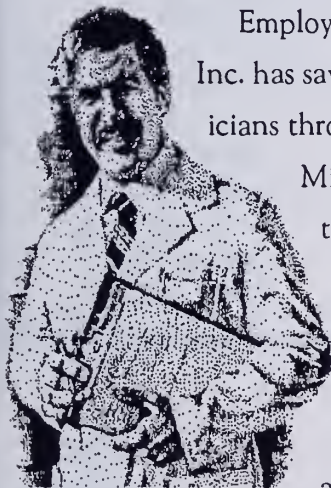
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### **New Members/*continued***

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**Payne, Patricia A.**, Greenville. Born Kosciusko, MS, January 28, 1947; MD, University of Mississippi School of Medicine, Jackson, MS, 1972; interned one year University of Pennsylvania Medical School Hospital, Philadelphia, PA 1972-73; pathology residency, University Medical Center, Jackson, MS, 1979-82; elected by Delta Medical Society.

**Psikogios, Michael L.**, Senatobia. Born Biloxi, MS, July

14, 1960; MD, University of Mississippi School of Medicine, Jackson, MS, 1987; interned one year, University of Tennessee, Memphis Medical Center, Memphis, TN; internal medicine residency, Methodist Hospital, Memphis, TN 1988-89 and 1991-92; elected by North Mississippi Medical Society.

**Tabatabali, Ashraf**, Picayune. Born Iran, April 21, 1950; MD, Tsfahan Medical School, Iran 1975; interned, same, one year; pediatrics residency, Lafayette Charity Hospital, Lafayette, LA, 1979-82; elected by Pearl River Medical Society. □

### **COMMENTS or QUERIES....**

The Editors of *Journal MSMA* invite you to comment on any material that appears in or is absent from the publication.

If you have a query or comment, please send it to:

The Editor,  
*Journal MSMA*,  
PO Box 5229,  
Jackson, MS  
39296-5229

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## **Deaths**

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**Ellis, Donald R.**, Clarksdale. Born Pickens Co, AL, September 10, 1920; MD, University of California Medical School 1944; interned one year Kings County Hospital, Brooklyn, NY; ob-gyn residency, Erlanger Hospital, Chattanooga, TN, 1/47-1/48; ob-gyn fellowship, Tulane University, New Orleans, LA, 1/48 - 6/49 & 6/50-3/51; died April 24, 1993, age 72.

**McBryde, Angus M.**, Sumrall. Born Purvis, MS, November 19, 1919; MD, Tulane University School of Medicine, New Orleans, LA, 1950; interned one year, U. S. Naval Hospital, Great Lakes, IL; died April 30, 1993, age 73.

**Williams, J Collins**, Greenville. Born Humboldt, TN, February 18, 1919; MD, University of Tennessee College of Medicine, Memphis, TN, 1950; interned one year Memphis Baptist Hospital and one year ob-gyn training John Gaston Hospital, Memphis, TN; died April 22, 1993, age 74. □



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AMMS

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Registration Deadline September 24, 1993

**Todd N. Adkins**, a first year fellow in the division of allergy and immunology, St Louis University School of Medicine, has received a \$25,000 Allergy Fellowship from the Allen and Hanburys Respiratory Institute. He earned his medical degree from the University of MS School of Medicine in 1988.

**Bryan Barksdale**, a Jackson cardiologist, was honored recently with an appreciation dinner hosted by many of the 550 heart patients

he has helped through the cardiac class at Jackson's Downtown YMCA.

**Walter Burnett** of Yazoo City has joined the staff of MEA Medical Clinics in Jackson.

**Ron Cannon** of Jackson has been elected to active fellowship in The American Laryngological, Rhinological, & Otolological Society also known as The Triological Society.

**Rickey Chance** of Laurel has joined the staff of MEA Medical Clinics in Laurel.

**Robert K. Collins**, of Mississippi State Mississippi, recently served as faculty for the symposium *Third Annual Southeastern Conference's Sports Medicine Symposium* sponsored by the Southern Medical Association (SMA) in conjunction with the Southern Orthopaedic Association.

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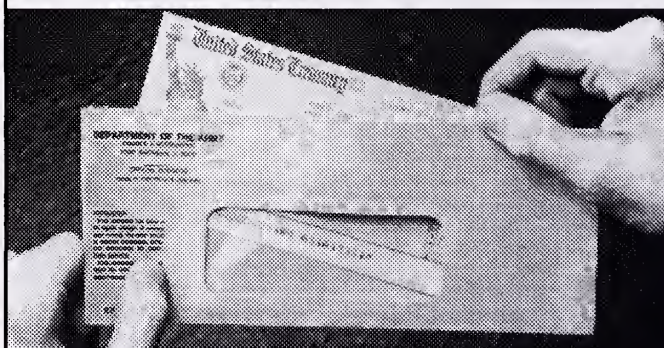
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**J. Robert Coltharp**, of Hattiesburg, recently received a three-year appointment as cancer liaison physician for the Hospital Cancer Program at Methodist Hospital. The program is part of the Commission on Cancer of the American College of Surgeons. Dr. Coltharp is among a national network of over 2,100 volunteer cancer liaison physicians who provide leadership and support of the program and other Commission on Cancer activities.

**Gary Davis** of Jackson has been elected secretary of the MS Nephrologic Society.

**Lawrence J. Derbes, Jr.**, has associated with the Southern Heart Center, in the practice of cardiology, 415 S. 28th Avenue, Hattiesburg.

**James W. Ervin, Jr.**, of Vicksburg, has completed continuing medical education requirements to retain active membership in the American Academy of Family Physicians.

**William C. Hopper, Jr.**, an orthopaedic surgeon from Gulfport, recently attended the seminar *Orthopaedic Update* in Point Clear Alabama.

**W. Briggs Hopson, Jr.**, a surgeon, recently met and discussed the latest procedures during the annual meeting of the Trauma Committee of the American College of Surgeons. Dr. Hopson is a senior member of the committee which is made up of about 50 physicians who formulate guidelines for trauma care in the United States.

**Wayne A. Hughes, Michael G. May** and **Samuel N. Crosby** announce the opening of The Family Practice Clinic, 110 Millsaps Drive, Methodist Hospital Medical Park, Hattiesburg. **Terry R. Lowe** will

join the Family Practice Clinic in early July.

**Walter E. Johnston**, of Vicksburg has completed continuing medical education requirements to retain active membership in the American Academy of Family Physicians.

**Bruce Longest**, of Bruce, announces the relocation of his office for the practice of family medicine to the Bruce Family Medical Center, Bruce Town Square.

**Robert D. McBroom**, of Pascagoula, announces the relocation of his office for the practice of internal medicine to 4105 Hospital Road, Medical Arts Building, Suite 110, Pascagoula.

**John R. Mitchell**, of Pontotoc was named Pontotoc Hospital's 1993 "Doctor of the Year" by hospital employees and staff members.

**Francis S. Morrison** of Jackson attended the recent meeting of the American Society for Apheresis in Boston, where he chaired a scientific session on Therapeutic Plasma exchange. During that meeting, he was named president-elect of the World Association of Apheresis.

**Marcelo J. Ruvinsky** of Jackson has been elected president of the MS Nephrologic Society.

**Buddy Savoie** of Jackson presented at the 12th Annual Meeting of the Arthroscopy Association of North America, in Palm Desert, CA, the following papers: *Comparison of Arthroscopic Debridement versus Open Full thickness Rotator Cuff Repair, Release of Flexion Contractures of The Elbow, and Arthroscopic Reconstruction of the Shoulder*. With **Larry Field**, he presented a paper on *Arthroscopic Repair of Shoulder Labral Detach-*

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*ment Lesions of the Shoulder: Techniques and Clinical Results* and with Beth Gasson, RN he present a paper on *Glove Puncture During Routine Arthroscopic Surgery*.

**Hildon H. Sessums Jr.**, a family physician in Vicksburg, has been certified by the Medical Review Officer Certification Council to evaluate drug and alcohol tests in public and private sectors of the workplace.

**Plez Tinsley, Jr.**, a facial plastic surgeon and ear, nose, and throat specialist from Meridian, recently attended the first mid-winter workshop on advances in cosmetic surgery sponsored by the American Academy of Facial Plastics and Reconstructive Surgery. At the course, Dr. Tinsley lectured as a member of the faculty on the subject of *Chemical Peels and Its Effect on the Aging Face*.

**Bill Walton** has associated with Rud Robison at the Saltillo Family Medical Clinic, 353 Mobile St., Saltillo.

**Abelardo S. Wee** has associated with **Roland T. Abangan** and **Kazuo Ugajin** of the Meridian Neurosurgical Clinic, PA, in the practice of neurology, 1020 - 22nd Avenue, Ste. 2, Meridian.

**Sidney Wong** of Gulfport recently attended the symposium *Fourth Annual Focus On The Female Patient* sponsored by the Southern Medical Association.

**Tom Wooldridge** of Tupelo has been elected vice-president of the MS Nephrologic Society. □

## Physicians' Recognition Award



Fifteen MSMA members were named recipients of the AMA Physicians Recognition Award in April 1993. This award is presented by the American Medical Association to Physicians who have voluntarily completed a specified number of continuing medical education hours. These individuals are presented below by Medical Society.

CENTRAL MEDICAL SOCIETY  
**Albert B. Britton, MD**  
**Vincent Liberto, MD**  
**Cynthia L. Undesser, MD**

NORTH CENTRAL MEDICAL SOCIETY  
**L. C. Henson, MD**

SOUTH CENTRAL MISSISSIPPI MEDICAL SOCIETY  
**Richard G. Burris, MD**  
**Fred J. McDonnell, MD**

COAST COUNTIES MEDICAL SOCIETY  
**Joe Mark Harris, MD**

NORTHEAST MISSISSIPPI MEDICAL SOCIETY  
**Robert E. Coghlan, MD**  
**D. Alan Pritchard, MD**

SOUTH MISSISSIPPI MEDICAL SOCIETY  
**Richmond L. Alexander, MD**  
**Stephen C. Lambert, MD**

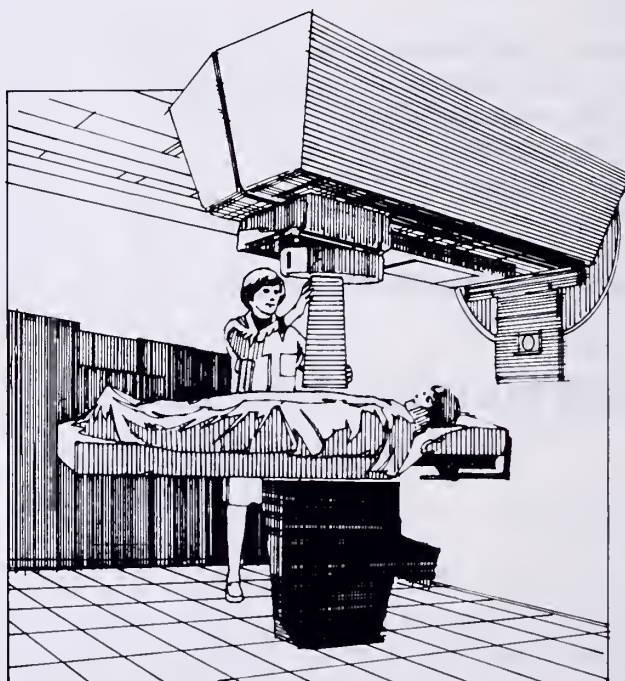
EAST MISSISSIPPI MEDICAL SOCIETY  
**Cheryl Gay Clark, MD**

SINGING RIVER MEDICAL SOCIETY  
**Gary H. Groff, MD**

WEST MISSISSIPPI MEDICAL SOCIETY  
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# Meetings

## NATIONAL AND REGIONAL

**American Medical Association**, Annual Meeting, June 13 - 17, 1993  
Chicago; Interim, December 5 - 8, New Orleans, LA James S. Todd,  
MD, Executive Vice President, 515 N. State St., Chicago, IL 60610

## STATE AND LOCAL

**Mississippi State Medical Association**, 126th Annual Session, May  
11-15, 1994, Jackson, Charles L. Mathews, Executive Director, 735  
Riverside Drive, PO Box 5229, Jackson 39296-5229.

**Mississippi Academy of Family Physicians**, Annual Meeting, July 28-  
31, 1993, Destin, FL. Leontine Stevens, Executive Secretary, PO Box  
1215 Ridgeland 39158.

**Amite-Wilkinson Counties Medical Society**, 3rd Monday, March, June,  
September, December, James S. Poole, MD, Secy., The Gloster Clinic,  
PO Box D, Gloster 39638. Counties: Amite, Wilkinson.

**Central Medical Society**, 1st Tuesday, February, April, October, De-  
cember, 6:30 p.m., Primos Northgate Restaurant, Jackson. Patsy  
Douglas, Executive Secy., 735 Riverside Dr., Jackson 39202. Coun-  
ties: Hinds, Leake, Madison, Rankin, Scott, Simpson.

**Clarksdale and Six Counties Medical Society**, 3rd Wednesday, April,  
and 1st Wednesday, November, 2:00 p.m., Clarksdale, Glen L.  
Wegener, MD, Secy., PO Box 430, Clarksdale, MS 38614-0430.  
Counties: Coahoma, Quitman, Tallahatchie, Tunica.

**Coast Counties Medical Society**, January, March, June, and November.  
James E. Clarkson, MD, Secy., Mail: Ms. Leslie Johnson, PO Box  
128, Biloxi 39533. Counties: Hancock, Harrison.

**Delta Medical Society**, 2nd Wednesday, April and October. Walter H.  
Rose, MD, Secy., 122 E. Baker St., Indianola 38751. Counties: Boli-  
var, Humphreys, Leflore, Sunflower, Washington, Yazoo.

**East Mississippi Medical Society**, 1st Tuesday, February, April, June,  
October, December. Charles L. Wilkinson, MD, Secy., Mail: Ms.  
Jenkins, PO Box 4053, West Station, Meridian 39305. Counties:  
Clarke, Kemper, Lauderdale, Neshoba, Newton, Winston.

**Homochitto Valley Medical Society**. Meetings scheduled quarterly,  
David G. Hall, MD, Secy., 150 Jeff Davis Blvd, Suite 130, Natchez  
39120. Counties: Adams, Jefferson.

**North Central District Medical Society**, 3rd Wednesday, March, June,  
September, January, Gary Holdiness, MD, 332 Hwy 12 W, Kosciusko  
39090. Counties: Attala, Carroll, Choctaw, Granada, Holmes, Mon-  
tgomery, Webster.

**Northeast Mississippi Medical Society**, 1st Thursday, March, June,  
September, December. Richard L. Heyer, Jr., MD, Secy., Mail: Ms.  
Shirley Irwin, PO Box 3294, Tupelo 38803-3294. Counties: Alcorn,  
Calhoun, Chickasaw, Itawamba, Lee, Monroe, Pontotoc, Prentiss,  
Tishomingo, Union.

**North Mississippi Medical Society**, 1st Thursday, April, September, and  
3rd Thursday, January. Catherine E. Gleason, MD, Secy., 1306 Belk  
Blvd., Oxford 38655. Counties: Benton, Lafayette, Marshall, Panola,  
Tate, Tippah, Yalobusha.

**Prairie Medical Society**, 2nd Tuesday, March, June, September, De-  
cember, Joseph S. Boggess, MD, Secy., 515 Willowbrook Rd., Co-  
lumbus, MS 39701. Counties: Clay, Oktibbeha, Noxubee, Lowndes.

**Singing River Medical Society**, Quarterly, December, March, June and  
September. Hal Moore, MD, Secy., Mail: Ms. Beverly Small, 3003  
Shortcut Rd, Pascagoula 39567. County: Jackson.

**South Central Mississippi Medical Society**, 2nd Tuesday, March, June,  
September, December. Julian T. Janes, Jr., MD, Secy., PO Box 1910,  
McComb 39648. Counties: Copiah, Franklin, Lawrence, Lincoln,  
Pike, Walthall.

**South Mississippi Medical Society**, 2nd Thursday, March, June, Sep-  
tember, December. William A. Whitehead, MD, 415 South 28th  
Ave., Hattiesburg 39401-7246. Counties: Covington, Forrest, George,  
Greene, Jasper, Jefferson Davis, Jones, Lamar, Marion, Perry, Smith,  
Wayne.

**West Mississippi Medical Society**, 2nd Tuesday, January, May, Sep-  
tember, November, 6:30 p.m. Maxwell's Restaurant, Vicksburg.  
Chester Masterson, MD, Secy., 1901 Mission 66, Vicksburg 39180.  
Counties: Issaquena, Sharkey, Warren.

## Mississippi Institutions and Organizations Accredited for Continuing Medical Education

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Medical Center  
Hospital Dr.  
Clarksdale, MS 38614

Forrest General Hospital  
Mamie Street and Highway 49 South  
Hattiesburg, MS 39401

Singing River Hospital  
2809 Denny Ave.  
Pascagoula, MS 39567

Mississippi Baptist Medical Center  
1225 N. State Street  
Jackson, MS 39202

Greenwood Leflore Hospital  
1401 River Rd.  
Greenwood, MS 38930

Gulf Coast Community Hospital  
180 DeBuys Rd.  
Biloxi, MS 39531

Memorial Hospital at Gulfport  
4500 13th St.  
Gulfport, MS 39501

Natchez Regional Medical Center  
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Natchez, MS 39120

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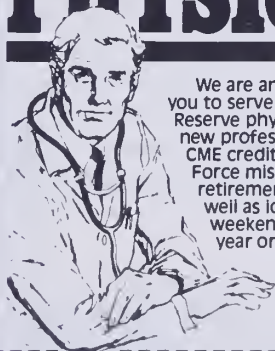
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## Index to Advertisers

Bristol-Myers Squibb Company - Pravachol .....	third and fourth cover
CancerPay Plus .....	218
CompHealth .....	194
Disability Determination .....	220
Doctors Insurance Reciprocal .....	208
Eli Lilly & Co. - Humulin .....	6
Employer Plus, Inc. ....	211
Hospice of Central Mississippi, Inc. ....	3 and 209
Medical Assurance Co. of MS .....	216
MMRC Home Health .....	second cover
MS Emergency Association .....	220
MS Physicians Insurance Company .....	186
MSMA Benefit Plan & Trust .....	197
Premier Printing .....	214
PRI-MED, Inc. ....	221
Southern Medical Association .....	213
The Doctors' Company .....	6
Trustmark .....	194
US Air Force .....	196
US Air Force Reserve .....	221
US Army Active .....	214
US Army Reserve .....	191



1. Jones PH, et al. Once-daily pravastatin in patients with primary hypercholesterolemia: a dose-response study. *Clin Cardiol*. 1991;14:146-151.

## PRAVACHOL® (Pravastatin Sodium Tablets)

### CONTRAINDICATIONS

hypersensitivity to any component of this medication.

Active liver disease or unexplained, persistent elevations in liver function tests (see WARNINGS).

**Pregnancy and lactation:** Atherosclerosis is a chronic process and discontinuation of lipid-lowering drugs during pregnancy should have little impact on the outcome of long-term therapy of primary hypercholesterolemia. Cholesterol and other products of cholesterol biosynthesis are essential components for fetal development (including synthesis of steroids and cell membranes). Since HMG-CoA reductase inhibitors decrease cholesterol synthesis and possibly the synthesis of other biologically active substances derived from cholesterol, they may cause fetal harm when administered to pregnant women. Therefore, HMG-CoA reductase inhibitors are contraindicated during pregnancy and in nursing mothers. **Pravastatin should be administered to women of childbearing age only when such patients are highly unlikely to conceive and have been informed of the potential hazards.** If the patient becomes pregnant while taking this class of drug, therapy should be discontinued and the patient apprised of the potential hazard to the fetus.

### WARNINGS

**Liver Enzymes:** HMG-CoA reductase inhibitors, like some other lipid-lowering therapies, have been associated with biochemical abnormalities of liver function. Increases of serum transaminase (ALT, AST) values to more than 3 times the upper limit of normal occurring on 2 or more (not necessarily sequential) occasions have been reported in 1.3% of patients treated with pravastatin in the U.S. over an average period of 18 months. These abnormalities were not associated with cholestasis and did not appear to be related to treatment duration. In those patients in whom these abnormalities were believed to be related to pravastatin and who were discontinued from therapy, the transaminase levels usually fell slowly to pretreatment levels. These biochemical findings are usually asymptomatic although worldwide experience indicates that anorexia, weakness, and/or abdominal pain may also be present in rare patients.

As with other lipid-lowering agents, liver function tests should be performed during therapy with pravastatin. Serum aminotransferases, including ALT (SGPT), should be monitored before treatment begins, every six weeks for the first three months, every eight weeks during the remainder of the first year, and periodically thereafter (e.g., at about six-month intervals). Special attention should be given to patients who develop increased transaminase levels. Liver function tests should be repeated to confirm an elevation and subsequently monitored at more frequent intervals. If increases in ALT and ALT equal or exceed three times the upper limit of normal and persist, then therapy should be discontinued. Persistence of significant aminotransferase elevations following discontinuation of therapy may warrant consideration of liver biopsy.

Active liver disease or unexplained transaminase elevations are contraindications to the use of pravastatin (see CONTRAINDICATIONS). Caution should be exercised when pravastatin is administered to patients with a history of liver disease or heavy alcohol ingestion (see CLINICAL PHARMACOLOGY: Pharmacokinetics/Pharmacokinetics). Such patients should be closely monitored, started at the lower end of the recommended dosing range, and titrated to the desired therapeutic effect.

**Skeletal Muscle: Rhabdomyolysis with renal dysfunction secondary to myoglobinuria has been reported with pravastatin and other drugs in this class.** Uncomplicated myalgia has also been reported in pravastatin-treated patients (see ADVERSE REACTIONS). Myopathy, defined as muscle aching or muscle weakness in conjunction with increases in creatine phosphokinase (CPK) values to greater than 10 times the upper limit of normal was reported to be possibly due to pravastatin in only one patient in clinical trials (<0.1%). Myopathy should be considered in any patient with diffuse myalgias, muscle tenderness or weakness, and/or marked elevation of CPK. Patients should be advised to report promptly unexplained muscle pain, tenderness or weakness, particularly if accompanied by malaise or fever. **Pravastatin therapy should be discontinued if markedly elevated CPK levels occur or myopathy is diagnosed or suspected.** Pravastatin therapy should also be temporarily withheld in any patient experiencing an acute or serious condition predisposing to the development of renal failure secondary to rhabdomyolysis, e.g., sepsis; hypotension; major surgery; trauma; severe metabolic, endocrine, or electrolyte disorders; or uncontrolled epilepsy.

The risk of myopathy during treatment with lovastatin is increased if therapy with either cyclosporine, gemfibrozil, erythromycin, or niacin is administered concurrently. There is no experience with the use of pravastatin together with cyclosporine. Myopathy has not been observed in clinical trials involving small numbers of patients who were treated with pravastatin together with niacin. One trial of limited size involving combined therapy with pravastatin and gemfibrozil showed a trend toward more frequent CPK elevations and patient withdrawals due to musculoskeletal symptoms in the group receiving combined treatment as compared with the groups receiving placebo, gemfibrozil, or pravastatin monotherapy. Myopathy was not reported in this trial (see PRECAUTIONS: Drug Interactions). One patient developed myopathy when clofibrate was added to a previously well tolerated regimen of pravastatin; the myopathy resolved when clofibrate therapy was stopped and pravastatin treatment continued. **The use of fibrates alone may occasionally be associated with myopathy. The combined use of pravastatin and fibrates should generally be avoided.**

### PRECAUTIONS

**General:** Pravastatin may elevate creatine phosphokinase and transaminase levels (see ADVERSE REACTIONS).

This should be considered in the differential diagnosis of chest pain in a patient on therapy with pravastatin.

**Homozygous Familial Hypercholesterolemia:** Pravastatin has not been evaluated in patients with rare homozygous familial hypercholesterolemia. In this group of patients, it has been reported that HMG-CoA reductase inhibitors are less effective because the patients lack functional LDL receptors.

**Renal Insufficiency:** A single 20 mg oral dose of pravastatin was administered to 24 patients with varying degrees of renal impairment (as determined by creatinine clearance). No effect was observed on the pharmacokinetics of pravastatin or its 3 $\alpha$ -hydroxy isomeric metabolite (SQ 31,906). A small increase was seen in mean AUC values and half-life (t<sub>1/2</sub>) for the inactive enzymatic ring hydrolysis metabolite (SQ 31,945). Given this small sample size, the dosage administered, and the degree of individual variability, patients with renal impairment who are receiving pravastatin should be closely monitored.

**Information for Patients:** Patients should be advised to report promptly unexplained muscle pain, tenderness or weakness, particularly if accompanied by malaise or fever.

**Drug Interactions:** Immunosuppressive Drugs, Gemfibrozil, Niacin (Nicotinic Acid), Erythromycin: See WARNINGS: Skeletal Muscle.

**Antipyrine:** Clearance by the cytochrome P450 system was unaltered by concomitant administration of pravastatin. Since pravastatin does not appear to induce hepatic drug-metabolizing enzymes, it is not expected that any significant interaction of pravastatin with other drugs (e.g., phenytoin, quinidine) metabolized by the cytochrome P450 system will occur.

**Cholestyramine/Colestipol:** Concomitant administration resulted in an approximately 40 to 50% decrease in the mean AUC of pravastatin. However, when pravastatin was administered 1 hour before or 4 hours after cholestyramine or 1 hour before colestipol and a standard meal, there was no clinically significant decrease in bioavailability or therapeutic effect. (See DOSAGE AND ADMINISTRATION: Concomitant Therapy.)

**Warfarin:** In a study involving 10 healthy male subjects given pravastatin and warfarin concomitantly for 6 days, bioavailability parameters at steady state for pravastatin (parent compound) were not altered. Pravastatin did not alter the plasma protein-binding of warfarin. Concomitant dosing did increase the AUC and C<sub>max</sub> of warfarin but did not produce any changes in its anticoagulant action (i.e., no increase was seen in mean prothrombin time after 6 days of concomitant therapy). However, bleeding and extreme prolongation of prothrombin time have been reported with another drug in this class. Patients receiving warfarin-type anticoagulants should have their prothrombin times closely monitored when pravastatin is initiated or the dosage of pravastatin is changed.

**Cimetidine:** The AUC<sub>0-12h</sub> for pravastatin when given with cimetidine was not significantly different from the AUC for pravastatin when given alone. A significant difference was observed between the AUC's for pravastatin when given with cimetidine compared to when administered with placebo.

**Digoxin:** In a crossover trial involving 16 healthy male subjects given pravastatin and digoxin concurrently for 9 days, the bioavailability parameters of digoxin were not affected. The AUC of pravastatin tended to increase, but the overall bioavailability of pravastatin plus its metabolites SQ 31,906 and SQ 31,945 was not altered.

**Gemfibrozil:** In a crossover study in 20 healthy male volunteers given concomitant single doses of pravastatin and gemfibrozil, there was a significant decrease in urinary excretion and protein binding of pravastatin. In addition, there was a significant increase in AUC, C<sub>max</sub>, and T<sub>max</sub> for the pravastatin metabolite SQ 31,906. Combination therapy with pravastatin and gemfibrozil is generally not recommended.

In interaction studies with aspirin, antacids [1 hour prior to PRAVACHOL (pravastatin sodium)], cimetidine, nicotinic acid, or probucol, no statistically significant differences in bioavailability were seen when PRAVACHOL was administered.

**Other Drugs:** During clinical trials, no noticeable drug interactions were reported when PRAVACHOL was added to diuretics, antihypertensives, digitalis, converting-enzyme inhibitors, calcium channel blockers, beta-blockers, or nitroglycerin.

**Endocrine Function:** HMG-CoA reductase inhibitors interfere with cholesterol synthesis and lower circulating cholesterol levels and, as such, might theoretically blunt adrenal or gonadal steroid hormone production. Results of clinical trials with pravastatin in males and post-menopausal females were inconsistent with regard to possible effects of the drug on basal steroid hormone levels. In a study of 21 males, the mean testosterone response to human chorionic gonadotropin was significantly reduced (p<0.004) after 16 weeks of treatment with 40 mg of pravastatin. However, the percentage of patients showing a  $\geq$ 50% rise in plasma testosterone after human chorionic gonadotropin stimulation did not change significantly after therapy in these patients. The effects of HMG-CoA reductase inhibitors on spermatogenesis and fertility have not been studied in adequate numbers of patients. The effects, if any, of pravastatin on the pituitary-gonadal axis in pre-menopausal females are unknown. Patients treated with pravastatin who display clinical evidence of endocrine dysfunction should be evaluated appropriately. Caution should also be exercised if an HMG-CoA reductase inhibitor or other agent used to lower cholesterol levels is administered to patients also receiving other drugs (e.g., ketoconazole, spironolactone, cimetidine) that may diminish the levels or activity of steroid hormones.

**CNS Toxicity:** CNS vascular lesions, characterized by perivascular hemorrhage and edema and mononuclear cell

infiltration of perivascular spaces, were seen in dogs treated with pravastatin at a dose of 25 mg/kg/day, a dose that produced a plasma drug level about 50 times higher than the mean drug level in humans taking 40 mg/day. Similar CNS vascular lesions have been observed with several other drugs in this class.

A chemically similar drug in this class produced optic nerve degeneration (Wallenian degeneration of retinogenicular fibers) in clinically normal dogs in a dose-dependent fashion starting at 60 mg/kg/day, a dose that produced mean plasma drug levels about 30 times higher than the mean drug level in humans taking the highest recommended dose (as measured by total enzyme inhibitory activity). This same drug also produced vestibulocochlear Wallenian-like degeneration and retinal ganglion cell chromatolysis in dogs treated for 14 weeks at 180 mg/kg/day, a dose which resulted in a mean plasma drug level similar to that seen with the 60 mg/kg/day dose.

**Carcinogenesis, Mutagenesis, Impairment of Fertility:** In a 2-year study in rats fed pravastatin at doses of 10, 30, or 100 mg/kg body weight, there was an increased incidence of hepatocellular carcinomas in males at the highest dose (p<0.01). Although rats were given up to 125 times the human dose (HD) on a mg/kg body weight basis, their serum drug levels were only 6 to 10 times higher than those measured in humans given 40 mg pravastatin as measured by AUC.

The oral administration of 10, 30, or 100 mg/kg (producing plasma drug levels approximately 0.5 to 5.0 times human drug levels at 40 mg) of pravastatin to mice for 22 months resulted in a statistically significant increase in the incidence of malignant lymphomas in treated females when all treatment groups were pooled and compared to controls (p<0.05). The incidence was not dose-related and male mice were not affected.

A chemically similar drug in this class was administered to mice for 72 weeks at 25, 100, and 400 mg/kg body weight, which resulted in mean serum drug levels approximately 3, 15, and 33 times higher than the mean human serum drug concentration (as total inhibitory activity) after a 40 mg oral dose. Liver carcinomas were significantly increased in high-dose females and mid- and high-dose males, with a maximum incidence of 30 percent in males. The incidence of adenomas of the liver was significantly increased in mid- and high-dose females. Drug treatment also significantly increased the incidence of lung adenomas in mid- and high-dose males and females. Adenomas of the eye Harderian gland (a gland of the eye of rodents) were significantly higher in high-dose mice than in controls.

No evidence of mutagenicity was observed *in vitro*, with or without rat liver metabolic activation, in the following studies: microbial mutagenesis tests, using mutant strains of *Salmonella typhimurium* or *Escherichia coli*, a forward mutation assay in L5178Y TK +/– mouse lymphoma cells, a chromosomal aberration test in hamster cells, and a gene conversion assay using *Saccharomyces cerevisiae*. In addition, there was no evidence of mutagenicity in either a dominant lethal test in mice or a micronucleus test in mice.

In a study in rats, with daily doses up to 500 mg/kg, pravastatin did not produce any adverse effects on fertility or general reproductive performance. However, in a study with another HMG-CoA reductase inhibitor, there was decreased fertility in male rats treated for 34 weeks at 25 mg/kg body weight, although this effect was not observed in a subsequent fertility study when this same dose was administered for 11 weeks (the entire cycle of spermatogenesis, including epididymal maturation). In rats treated with this same reductase inhibitor at 180 mg/kg/day, seminiferous tubule degeneration (necrosis and loss of spermatogenic epithelium) was observed. Although not seen with pravastatin, two similar drugs in this class caused drug-related testicular atrophy, decreased spermatogenesis, spermatocytic degeneration, and giant cell formation in dogs. The clinical significance of these findings is unclear.

**Pregnancy: Pregnancy Category X:** See CONTRAINDICATIONS.

Safety in pregnant women has not been established. Pravastatin was not teratogenic in rats at doses up to 1000 mg/kg daily or in rabbits at doses of up to 50 mg/kg daily. These doses resulted in 20x (rabbit) or 240x (rat) the human exposure based on surface area (mg/meter<sup>2</sup>). However, in studies with another HMG-CoA reductase inhibitor, skeletal malformations were observed in rats and mice. PRAVACHOL (pravastatin sodium) should be administered to women of child-bearing potential only when such patients are highly unlikely to conceive and have been informed of the potential hazards. If the woman becomes pregnant while taking PRAVACHOL, it should be discontinued and the patient advised again as to the potential hazards to the fetus.

**Nursing Mothers:** A small amount of pravastatin is excreted in human breast milk. Because of the potential for serious adverse reactions in nursing infants, women taking PRAVACHOL should not nurse (see CONTRAINDICATIONS).

**Pediatric Use:** Safety and effectiveness in individuals less than 18 years old have not been established. Hence, treatment in patients less than 18 years old is not recommended at this time. (See also PRECAUTIONS: General.)

### ADVERSE REACTIONS

Pravastatin is generally well tolerated, adverse reactions have usually been mild and transient. In 4-month long placebo-controlled trials, 1.7% of pravastatin-treated patients and 1.2% of placebo-treated patients were discontinued from treatment because of adverse experiences attributed to study drug therapy, this difference was not statistically significant. In long-term studies, the most common reasons for discontinuation were asymptomatic serum transaminase increases and mild, non-specific gastrointestinal complaints. During clinical trials the overall incidence of adverse events in the elderly was not different from the incidence observed in younger patients.

**Adverse Clinical Events:** All adverse clinical events (regardless of attribution) reported in more than 2% of pravastatin-treated patients in the placebo-controlled trials are identified in the table below, also shown are the percentages of patients in whom these medical events were believed to be related or possibly related to the drug

Body System/Event	All Events %		Events Attributed to Study Drug %	
	Pravastatin (N=900)	Placebo (N=411)	Pravastatin (N=900)	Placebo (N=411)
Cardiovascular				
Cardiac Chest Pain	4.0	3.4	0.1	0.0
Dermatologic				
Rash	4.0*	1.1	1.3	0.9
Gastrointestinal				
Nausea/Vomiting	7.3	7.1	2.9	3.4
Diarrhea	6.2	5.6	2.0	1.9
Abdominal Pain	5.4	6.9	2.0	3.9
Constipation	4.0	7.1	2.4	5.1
Flatulence	3.3	3.6	2.7	3.4
Heartburn	2.9	1.9	2.0	0.7
General				
Fatigue	3.8	3.4	1.9	1.0
Chest Pain	3.7	1.9	0.3	0.2
Influenza	2.4*	0.7	0.0	0.0
Musculoskeletal				
Localized Pain	10.0	9.0	1.4	1.5
Myalgia	2.7	1.0	0.6	0.0
Nervous System				
Headache	6.2	3.9	1.7*	0.2
Dizziness	3.3	3.2	1.0	0.5
Renal/Genitourinary				
Urinary Abnormality	2.4	2.9	0.7	1.2
Respiratory				
Common Cold	7.0	6.3	0.0	0.0
Rhinitis	4.0	4.1	0.0	0.0
Cough	2.6	1.7	0.1	0.0

\*Statistically significantly different from placebo.

The following effects have been reported with drugs in this class:

**Skeletal:** myopathy, rhabdomyolysis.

**Neurological:** dysfunction of certain cranial nerves (including alteration of taste, impairment of extra-ocular movements, facial paresis), tremor, vertigo, memory loss, paresthesia, peripheral neuropathy, peripheral nerve palsy.

**Hypersensitivity Reactions:** An apparent hypersensitivity syndrome has been reported rarely which has included one or more of the following features: anaphylaxis, angioedema, lupus erythematosus-like syndrome, polymyalgia rheumatica, vasculitis, purpura, thrombocytopenia, leukopenia, hemolytic anemia, positive ANA, ESR increase, arthritis, arthralgia, urticaria, asthenia, photosensitivity, fever, chills, flushing, malaise, dyspnea, toxic epidermal necrolysis, erythema multiforme, including Stevens-Johnson syndrome.

**Gastrointestinal:** pancreatitis, hepatitis, including chronic active hepatitis, cholestatic jaundice, fatty change in liver, and, rarely, cirrhosis, fulminant hepatic necrosis, and hepatoma, anorexia, vomiting.

**Reproductive:** gynecomastia, loss of libido, erectile dysfunction.

**Eye:** progression of cataracts (lens opacities), ophthalmoplegia.

**Laboratory Test Abnormalities:** Increases in serum transaminase (ALT, AST) values and CPK have been observed (see WARNINGS).

Transient, asymptomatic eosinophilia has been reported. Eosinophil counts usually returned to normal despite continued therapy. Anemia, thrombocytopenia, and leukopenia have been reported with other HMG-CoA reductase inhibitors.

**Concomitant Therapy:** Pravastatin has been administered concurrently with cholestyramine, colestipol, nicotinic acid, probucol and gemfibrozil. Preliminary data suggest that the addition of either probucol or gemfibrozil to therapy with lovastatin or pravastatin is not associated with greater reduction in LDL cholesterol than that achieved with lovastatin or pravastatin alone. No adverse reactions unique to the combination or in addition to those previously reported for each drug alone have been reported. Myopathy and rhabdomyolysis (with or without acute renal failure) have been reported when another HMG-CoA reductase inhibitor was used in combination with immunosuppressive drugs, gemfibrozil, erythromycin, or lipid lowering doses of nicotinic acid. Concomitant therapy with HMG-CoA reductase inhibitors and these agents is generally not recommended. (See WARNINGS: Skeletal Muscle and PRECAUTIONS: Drug Interactions.)

### OVERDOSAGE

There have been no reports of overdoses with pravastatin.

Should an accidental overdose occur, treat symptomatically and institute supportive measures as required.



THE PRAVACHOL® DIRECTION  
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**PRAVACHOL®**  
pravastatin sodium 20 mg tablets

PRAVACHOL is indicated as an adjunct to diet for the reduction of elevated total and LDL-cholesterol levels in patients with primary hypercholesterolemia (Types IIa and IIb) when the response to diet alone has not been adequate. Active liver disease or unexplained transaminase elevations, pregnancy and lactation are contraindications to the use of pravastatin sodium.

Please see CONTRAINDICATIONS, WARNINGS, PRECAUTIONS, and ADVERSE REACTIONS in the brief summary of prescribing information on the adjacent page.



Bristol-Myers Squibb Company



# JOURNAL



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# JOURNAL

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## SCIENTIFIC ARTICLES

- Degenerative Cervical Disc Disease** 223  
*Robert A McGuire, MD*
- Clinicopathologic Conference II** 227  
*Joe C. Files, MD, Editor, et al*

## SPECIAL ARTICLES

- Hospice Care** 233  
*David N. Duddleston, MD and Linda Edwards*
- New Charitable Immunity Law** 235

## EDITORIALS

- "The Devil Is In The Details"** 238  
*Don Q. Mitchell, MD*
- You Know The Plan Is In Trouble When She Comes To The AMA** 239  
*Leslie E. England, MD, Associate Editor*

## DEPARTMENTS

- Comments** 241
- Medical Organization** 243
- New Members** 251
- Deaths** 251
- Personals** 253
- Placement Service** 256
- Classified** 258

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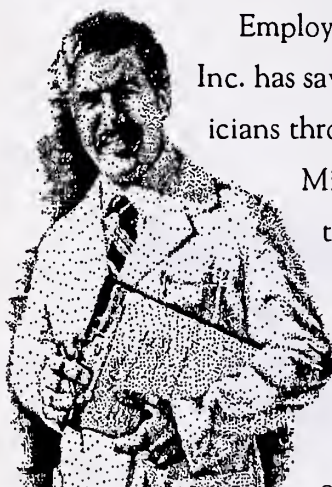
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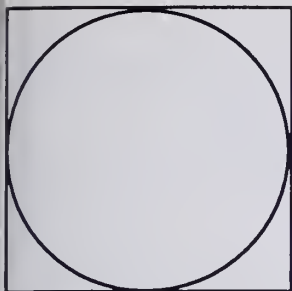


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# Family Violence And Sexual Assault: The Health Care Response

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## Agenda

### Thursday, August 26

8:00 - 9:30 Registration

9:30 - 10:45 Workshop I

10:45 - 11:00 Break

11:00 - 12:15 Workshop II

12:15 - 1:45 Luncheon Session

*Keynote Speaker • Mary Krueger, PhD*

Emory University

1:45 - 3:00 Workshop III

3:00 - 3:15 Break

3:15 - 4:30 Workshop IV

### Friday, August 27

8:30 - 10:00 Workshop V

General Session

10:00 - 10:15 Break

10:15 - 11:45 Workshop VI

General Session

(The conference agenda includes 10 separate workshops. See workshop schedule to plan your conference schedule.)

## Workshop Schedule

### Thursday, August 26

Please mark your workshop choice for each session.

#### 9:30 - 10:45 Workshop I

\_\_\_ Dynamics of Family Violence • *Mary Krueger, PhD*

\_\_\_ Special Needs of the Sexual Assault Victim • *Jane Philo, RN*

#### 11:00 - 12:15 Workshop II

\_\_\_ Identification & Assessment of Battered Women In the Emergency Department • *Debrynda Davey, EdD, RN*

\_\_\_ Sexual Assault Within the Family • *Mary Krueger, PhD*

#### 1:45 - 3:00 Workshop III

\_\_\_ Violence in Youth • *Robert Smith, MD*

\_\_\_ Medical Perspectives in Dealing With Victims of Sexual Assault • *Diane Beebe, MD*

#### 3:45 - 4:30 Workshop IV

\_\_\_ Battered Pregnant Women: Identification, Management, & Empowerment • *Lynn Glass-Heidenrich, RN*

\_\_\_ Collection & Preservation of Evidence in Sexual Assault Cases • *Deborah Haller, BS*

## Family Violence And Sexual Assault: The Health Care Response

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**Conference Registration Fees: Physicians - \$100 • General Registration - \$50 • Students/Volunteers - \$35.**

Please return with appropriate registration fee (check or money orders only) payable to the Mississippi State Coalition Against Domestic Violence (MSCADV) by August 16. The registration fee includes materials, refreshments, and Thursday luncheon. On-site registration after August 16 is an additional \$15 above the appropriate registration fee. For more information call Lark Johnson at 601/638-0555.

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## Degenerative Cervical Disc Disease

ROBERT A. MCGUIRE, JR, MD

### PATHOPHYSIOLOGY

Cervical spondylosis refers to the changes occurring in the intervertebral disc, facet joints and joint of Luschka.(Figure 1) Changes within the disc that occur with ageing can lead to loss of the mechanical properties of the spinal seg-

ment with resultant symptomatology.<sup>1</sup> This loss of mechanical stability secondary to abnormal segmental dysfunction can lead to localized neck pain, referred pain into the interscapular, shoulder, arm and suboccipital areas, and occipital headache. These symptoms can be reproduced by injecting hypertonic saline into the disc and supraspinous ligament and may not necessarily arise due to direct nerve root irritation.

Cervical radiculopathy on the other hand refers to the signs and symptoms occurring as a direct result of nerve root compression. Radiculopathy occurs most frequently secondary to posterolateral disc herniation or spondylitic changes of the neurocentral joints of Luschka resulting in neuro-foraminal stenosis.(Figure 2)

Myelopathy usually results from long standing spondylosis narrowing the anteroposterior di-



Figure 1. This lateral radiograph reveals loss of disc height at multiple levels with osteophyte formation and loss of the normal cervical lordosis. This is a very typical picture of end stage disc changes that occur during the normal ageing process.



Figure 2. This MRI reveals a right posterolateral disc herniation impinging the exiting nerve root which can result in radiculopathy.



*Figure 3. This lateral myelogram exhibits significant narrowing of the spinal canal with resulting compression of the spinal cord. This can lead to upper motor involvement and present clinically as myelopathy.*

iameter of the spinal canal causing intrinsic change within the spinal cord tissues. (Figure 3) Myelopathy may also present with a significant radicular component, but will usually have evidence of associated upper motor neuron involvement. Clarke and Robinson showed in their series of cervical myelopathy that 75% of patients had episodic symptoms, 20% slowly progressed and 5% exhibited acute deterioration.<sup>2</sup>

### NATURAL HISTORY

Most cases of cervical radiculopathy rarely progress to myelopathy. Lees and Turner report 66% of patients treated nonoperatively have persistent symptoms.<sup>3</sup> Depalma reports in his series a 45% satisfactory result with nonoperative treatment.<sup>4</sup> Twenty-three percent of the failures were so disabled by their pain they were unable to return to their previous occupa-

tion. Gore's study of conservative treatment reveals 43% being pain free with 32% of patients reporting moderate to severe pain.<sup>5</sup> This represents a significant contrast to nonoperative treatment of lumbar spine pain which results in satisfactory outcome in 80-90% of patients at three months.<sup>6</sup>

### SIGNS AND SYMPTOMS

The presenting symptom in most cases will be pain. Neck pain may be localized in the neck, the shoulder, the arm or referred to the interscapular area. Radiculopathy presents with intense arm pain and minimal neck pain. Patients with myelopathy will generally complain of vague cervical and interscapular pain and in those cases exhibiting associated root entrapment, arm pain as well.<sup>7</sup>

With radiculopathy the complaint of pain will be along unilateral dermatomal patterns with weakness noted in muscles innervated by a single root. Patients with myelopathy will usually complain of generalized bilateral weakness rather than unilateral as seen in those with radiculopathy. Myelopathic patients will often exhibit gait disturbances, loss of fine motor dexterity and complain of bowel and bladder dysfunction.

Physical examination reveals deficits in both motor and sensory patterns of specific roots in those patients with radiculopathy whereas the weakness is generalized and symmetric in those with myelopathy. Deep tendon reflexes elicited in patients with myelopathy are hyperactive indicating upper motor neuron lesions. With radiculopathy, reflexes tend to be hypo active which is indicative of lower motor neuron involvement. Hoffman's sign, ankle clonus,

and Babinski's pathologic reflex all of which indicate cord involvement may be present in myelopathy. Provocative tests are helpful in diagnosing radiculo-pathy by reproducing the pain clinically.<sup>8</sup> Valsalva and cervical compression often reproduce the root pain which can be transiently relieved with cervical distraction. Spurling's maneuver which hyperextends and laterally rotates the cervical spine, will usually reproduce the radiculopathy. An excellent indicator of radiculopathy is the relief of arm pain with the shoulder abduction test. This alleviates nerve root tension in the upper extremity similar to flexing the hip and knee in the lower extremity to alleviate sciatic pain. Lhermitte's sign is the sensation of generalized electric shock elicited by forward flexion of the cervical spine in those patient with myelopathy.

### IMAGING

Obtaining AP, oblique and lateral flexion - extension radiographs provides excellent information about the cervical spine. This series provides information on alignment, disc space height, osteophyte formation, stability, and foraminal patency. From these radiographs one can assess the canal diameter using Torg's ratio. (Figure 4) This is obtained by measuring the canal distance from midbody to the laminar line divided by the width of the cervical vertebral body. A ratio of less than or equal to 0.8 indicates cervical stenosis.<sup>9</sup> Narrowing of the bony canal can lead to compression of the neural elements and development of myelopathy.

Magnetic resonance imaging, computed tomography and CT myelography are available for anatomically evaluating nerve





*Figure 4. A lateral radiograph can give significant information relating to space available for the spinal cord. A Torg ratio of less than 0.8 indicates cervical canal stenosis.*

root impingement, cord compression, and disc degeneration. The MRI is noninvasive and provides an excellent evaluation of the soft tissue structures of the cervical spine. CT scanning using 1 mm sections provides excellent data concerning the bony structures and soft tissues that lead to foraminal encroachment. A myelogram followed by CT scan yield excellent information on extradural, intradural, and intramedullary lesions of the cervical spine.

One must be careful in evaluating the results of these studies. Signs and symptoms must be correlated with the study to minimize false-positive results. Boden et al recently reported a 19% incidence of abnormal scans found in asymptomatic patients.<sup>10</sup>

#### **DIFFERENTIAL DIAGNOSIS**

When a patient presents with neck and arm pain, one must consider cervical spondylosis, cervical radiculopathy, cervical myelopathy, tumor, peripheral

nerve entrapment syndromes, thoracic outlet syndrome, brachial plexus disorders, shoulder disease and referred anginal pain. Most commonly seen are cervical spondylosis, radiculopathy and myelopathy.

Cervical spondylosis usually presents in the fifth or sixth decade with complaints of neck pain. Occasionally distal arm and referred shoulder pain is noted. Neurological examination is normal, but range of motion of the cervical spine may be restricted. Radiographically, disc narrowing over several levels with spurring, normal sagittal diameter and no instability is evident. MRI evaluation will reveal multi-level disc degeneration.

Cervical radiculopathy occurs in the younger patient with variable physical findings. Ventral compression of the rootlet may produce only motor disturbances, dorsal compression only sensory disturbances, but more often a combination of the two resulting in both motor and sensory involvement. The shoulder abduction test should relieve arm pain while Spurling's maneuver or Valsalva may provoke pain. MRI or myelogram-CT should confirm specific root involvement correlating with the physical exam.

Vague symptomatology and absence of hard neurological finding early, often lead to a delayed diagnosis of myelopathy. Subtle changes in gait, loss of fine motor movements, and upper extremity numbness must be thoroughly evaluated. MRI or myelogram-CT will reveal narrowing of the spinal canal with subsequent compression of the spinal cord which may ultimately induce intrinsic changes of the cord tissue itself. Prognosis for recovery is dependent upon early diagnosis and treatment.

#### **CONSERVATIVE TREATMENT**

Unless myelopathy is present, individuals with neck and arm pain not related to fracture or trauma should have a nonoperative period of care consisting of immobilization with a soft collar, nonsteroidal anti-inflammatory and analgesic medication.<sup>11</sup> Physical therapy consisting of ice, moist heat and ultra sound are helpful in the acute phase to alleviate pain and spasm. Cervical traction used appropriately is also helpful, but care must be utilized as inappropriate positioning can make the pain worse. Manipulation must be considered carefully as reported cases of neural deficit have occurred with its use. Patient education with reference to posture and lifting mechanics is included with early physical therapy.

#### **OPERATIVE TREATMENT**

Following failure of conservative measures or a progressive



*Figure 5. This lateral radiograph reveals a tricortical section of iliac crest placed in the C5-6 interspace. Note the reconstitution of disc height and realignment. This can lead to indirect decompression of the nerve root by enlarging the foramen for the exiting nerve root.*

neurologic deficit, surgical treatment is indicated. Anterior cervical discectomy with fusion is usually the procedure of choice. Several variations exist, but all utilize a bone plug to reestablish disc height indirectly decompressing the neural foramen. (Figure 5) Should significant foraminal stenosis be present, the hypertrophied uncinate process is removed with a power drill or micro surgical instruments. Single level procedures result in 80-90% satisfactory pain relief and 95% successful fusion.<sup>12</sup> Early results of multiple level procedures appear to favor the use of internal fixation.<sup>13</sup>

Surgical treatment for myelopathy includes anterior decompression and fusion using either multiple interbody fusions or vertebrectomy and strut grafting, expansible laminoplasty, or cervical laminectomy.<sup>14</sup> For two level disease, an anterior procedure is recommended. (Figure 6) Multi level disease can be treated



Figure 6. This radiograph reveals the postoperative appearance following the removal of a vertebral body and the disc on adjacent sides. This provides a method to completely decompress the neural tissues and stabilize the spine in a single stage.

posteriorly with laminoplasty provided the cervical spine is not kyphotic. Laminoplasty involves incising the laminae on one side at the lamina-facet junction then hinging open on the opposite side through a thinned cortical defect in the lamina. Laminectomy must be carefully considered in this population due to loss of normal lordosis. With cervical kyphosis, the spinal cord is stretched over the posterior aspect of the vertebral body and osteophytes. In this situation, compression of the spinal cord will not be relieved with removal of the laminae and may be exacerbated should further post-surgical kyphosis develop.

### SUMMARY

Degenerative cervical disc disease is a very common problem with most problems being resolved with conservative measures. Patients can present with a wide variation of complaints from neck pain to myelopathy secondary to spinal cord compression. In those patients requiring surgery for arm pain and myelopathy, the results are quite favorable. □

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**CASE RECORDS  
OF THE  
DEPARTMENT OF MEDICINE  
UNIVERSITY OF MISSISSIPPI  
MEDICAL CENTER**

**Clinicopathologic Conference II**

**Selection and Preparation:**

**Todd Adkins, MD**

**Matt Rees, MD**

**Francesco Simeone, MD**

**Joe C. Files, MD, *Editor***

**Differential Diagnosis: Joe C. Files, MD**

**Radiological Findings: Jennifer Hamrick-  
Turner, MD**

**Pathological Findings: Sue D. Walker, MD**

**CASE PRESENTATION**

A 39 year old white female was in her usual state of good health until August, 1989, when she began having trouble with menorrhagia and was noted to be anemic with a hemoglobin of 6.8 and a hematocrit of 23.8. She was diagnosed as having dysfunctional uterine bleeding and was placed on Provera without any appreciable response. She was admitted to the University Hospital in September, 1989, and was treated with I.V. Premarin with subsequent decrease of her menstrual bleeding. At that time she was placed on oral contraceptives and discharged. She was then followed by her local gynecologist and was noted to develop anemia secondary to severe menorrhagia. She was also noted to have fevers in the evenings. She was transfused three units of packed red blood cells and underwent a total abdominal hysterectomy and incidental appendectomy. Pathological examination of the uterus revealed chronic cervicitis and a secretory endometrium with endometritis and cystic degeneration. The patient's post-op course was uneventful except for temperature spikes to 101 in the afternoon without symptoms or signs of infec-

tion. An ANA was obtained which was positive with a titer of 1:40. She was discharged home for further evaluation as an outpatient.

In December, 1990, the patient underwent a CT scan of the abdomen at another institution and was found to have bilateral pleural effusions and an enlarged liver which was uniform in appearance, moderate splenomegaly, and diffuse ascites. She was noted to have a large, irregular mass in the lower pole of the left kidney, and at that time she was referred to University Hospital for further evaluation. She was initially seen at University Hospital on December 20, 1990, where she described progressive fatigue and a 20 pound weight loss over four months. She had a good appetite, but stated that she had post prandial bloating for several weeks and has had 5-6 loose water stools per day without blood or mucus. She also described late afternoon temperature spikes and occasional night sweats. She noted urinary frequency but denied dysuria, abdominal flank pain, or hematuria. A renal ultrasound done that day showed increased echogenicity bilaterally compatible with parenchymal disease. Also noted was a large hypoechoic solid mass measuring 8cm in diameter on the inferior pole of the left kidney. She was offered admission at that time but opted to wait until after the holidays. She was admitted to the University Hospital on December 26, 1990.

Physical exam at that time revealed a temperature of 99.0, blood pressure 138/88, pulse of 120, and a respiratory rate of 20. She weighed 66.1 kg. She was noted to be a well developed, well nourished white female. Examination of the head and neck region was unremarkable. Her cardiac exam was significant for an increased heart rate and a 1/6 systolic ejection murmur at the left lower sternal border which did not radiate. Lung examination was unremarkable. Examination of the abdomen revealed a protuberant abdomen that demonstrated shifting dullness and a fluid wave. Her liver span was percussed to 17cm in the right mid-clavicular line and splenomegaly was detected. The patient was not noted to have adenopathy. Her physical examination was otherwise unremarkable except for one plus pedal edema. Admission laboratory done at the time revealed a white count of 10,000 with 78% segs, 17 lymphs and 1 band. Hematocrit was 17.7 with an MCV of 72.7, an RDW of 15, and a platelet count of 619,000. PT, PTT: 13.7, 33.1. ESR >150. Electrolytes and renal panel were normal except for a BUN of 24 and a creatinine of 1.8. Other laboratory included a uric acid of 7.8, total protein of 4.3, total bilirubin of 0.3, a cal-

cium of 7.4, albumin of 1.6, direct bilirubin of .3, an LDH of 247, phosphate of 4.2, alk phos of 290, a GOT of 210, CPK of 26, iron 15, iron binding capacity of 157, and a ferritin of 59. Urinalysis revealed two white cells and one red cell per high powered field. She had 100mg/deciliter proteinuria and a pH of 6.0 with a specific gravity of 1.007. Examination of stool at that time was negative for white cells and OCPs, and a fat stain was also negative. A chest x-ray was remarkable for a 3cm left hilar mass and a 1.5cm soft tissue mass in the right mid lung field.

A 24 hour urine documented 47gm of proteinuria and a creatinine clearance of 25ml/minute. CT scan of the chest revealed multiple bilateral pulmonary nodules and prominent bilateral hilar regions. She had daily afternoon temperature elevations from 100.5 to 101. During the course of hospitalization, the patient's renal function markedly deteriorated despite maintenance of good urine output. At that time two separate diagnostic procedures were performed.

**Dr. Files:** I am going to make the assumption that this diagnosis is not necessarily in the field of my sub-specialty. I will review the points that I think are significant in the history and in the physical findings, and then we will approach a differential and see if we come up with the correct diagnosis. Dr. Turner, will you present the x-ray findings?

**Dr. Turner:** This is the patient's admission chest x-ray. The most striking thing about the film is this increased soft tissue density in the left hilar region that would be very suspicious for a mass. In addition, there is a soft tissue nodular within the lung parenchyma. I have some images from the CT chest exam. These are the mediastinal windows that demonstrate some increased tissue in the hilar region. This soft tissue density would be highly suspicious for lymphadenopathy. Contrast wasn't given because of the patient's renal status, so it diminishes the sensitivity somewhat. The next two images show the mediastinal windows and this is the nodular density that we were seeing on the plain chest film. It's about 1 - 1.5cm in size. In addition, you can see there are some other smaller soft tissue nodules that weren't apparent from the plain chest films radiograph. The next image that we have also showed these additional nodules in a subpleural location. This is the renal ultrasound. This is the normal appearing contour of the left kidney. We have a cut off the normal contour by

an abnormal mass. It contains echos throughout. You can see this is a little bit of the normal renal contour and there's a bulge in that contour with a roughly 8 x 6cm mass projecting off the lower pole that again is obviously a solid mass and contains echos. The right kidney was felt to be within normal limits in size but did show some increased echogenicity which is a fairly nonspecific finding you can see with multiple disease processes. That's all the radiology findings that we have.

**Dr. Files:** Can you tell from the CT chest if these nodules could be pulmonary infarction or does this look more like tumor?

**Dr. Turner:** It looks more like a soft tissue nodule to me as opposed to infarction because it's very discreet and it's very well defined and I would go with this being a soft tissue nodule.

Audience question: Does the patient have any skin rashes of any kind?

None that are reported in the chart.

**Dr. Files:** We hope that would have been reported in the chart. Does anyone else want to know anymore lab? I would have liked to have had two more bits of lab data. I think that there are four significant points to consider in figuring out this case. Number one: There's a renal mass with pulmonary nodules, and I think that most likely those nodules are related to the renal mass. Number two: There are B symptoms which we mentioned which are weight loss, fever, and night sweats. Number three: The patient has nephrotic syndrome. I probably should have put hepatosplenomegaly up there, but I did not. Number four: There is a diarrheal syndrome that I listed as secretory diarrhea.

If we look at renal masses, the first division to make in renal masses is whether it's solid or cystic. And the ultrasound clearly defined that this was not a cystic mass, but that it was a solid mass. The tumors are divided as to whether they are benign primary tumors or whether they are malignant primary tumors or whether they are secondary malignant tumors. Adenomas are the most common renal masses that are seen. If they are less than 3cm in size, they almost never cause metastatic disease. If they are above 3cm of size, they often metastasize. That sounds like it's a malignancy. Histologically it appears benign even though it may act malignant. The other tumors are extremely rare and would not show metastatic lesions to the lung.



The most common malignant tumor involving the kidney is adenocarcinoma or renal cell carcinoma, or hypernephroma - all names are interchangeable. They account for 85% of the malignant renal tumors. It has been called the internist's tumor in the past because of the many paraneoplastic phenomena that we see. We would certainly not think this is a Wilm's tumor in a patient that is 40 years of age. The other carcinomas are of the collecting system and the pelvis and this does not look like it arose from those sites. Sarcomas are extremely rare and I don't know of any differentiating point. Secondary tumors can involve or extend metastatically to the kidney. I have seen several patients with Hodgkin's disease and non-Hodgkin's lymphoma have renal involvement. There are renal complications of multiple myeloma as well as occasional leukemic movement of the kidney.

If you look at the systemic manifestations of renal cell carcinoma, we have many of the findings that we saw in this patient. We have fever, weight loss, and anemia. One can have erythrocytosis in 3-5% of the patients, and that's one of the things we always look for if we have someone that presents with an elevated red cell mass that does not have P-vera. They can have thrombocytosis, hypercalcemia, hypertension, Cushing's, galactorrhea, or amyloidosis. They can have migratory thrombophlebitis. They can get inferior vena cava obstruction from clot. These are associated syndromes, as well. How common are these things? The hematuria, which is a very common complaint in renal cell, happens at least 50% of the time. Abdominal masses that are palpable are found in a fourth of the patients. Anemia is present fairly significantly and you can see that as you go down the list, these all get less prevalent. There is a syndrome of hepatic dysfunction unrelated to metastatic spread with individuals who have renal cell carcinoma. If the tumor can be resected, nearly all of these symptoms will go away. The classic triad that we are all taught in medical school that points to renal cell carcinoma is hematuria, flank pain, and a mass. This happens in no more than 10% of the patients. Besides the mass effect of hypernephromas, you can get hypertension. You can get amyloidosis. You can get hypertension. You can get renal vein thrombosis, and you can bleed into the capsule of the kidney.

Complications that we want to discuss are those that are remote from the neoplasm itself. Those are nephrotic syndrome and amyloidosis. Nephrotic syndrome can be associated with carcinoma, with Hodgkin's disease, or with

nonHodgkin's lymphoma. We are going to assume that the primary lesion is in the kidney. If you look at neoplasia and nephrotic syndrome, in patients with carcinomas there are membranous glomerulonephropathies that are thought to be antigen antibody mediated in the majority of patients. In Hodgkin's disease, it is not the same histological finding. It is minimal change disease - Neil's disease. No one is sure exactly the etiology of the nephrotic syndrome in that clinical situation but the disease is thought to be mediated by abnormal T-cell function. Amyloidosis used to be a very common finding in late stage Hodgkin's disease, but is much less frequent now than it was in the past. The antigen antibody system causes the nephrotic syndromes associated with these malignancies. Tumor antigens are almost always found in the antigen antibody complex within the glomeruli.

Now, when we look at causes of diarrhea and corresponding secretory stimuli, I did not get a lot of help in evaluating this particular clinical problem. We know there was not a travel history and we know she was not abusing laxatives. We do not think she had VIP because her electrolytes were normal. We have no reason to think medullary carcinoma of the thyroid. She had nothing that went with carcinoid syndrome, she had nothing that went with ZE, and she had nothing that pointed to a villous adenoma of the rectum. She did not have anything that pointed to small bowel obstruction. She did have portal hypertension and severe hypoalbuminemia and I assume that with the change in oncotic pressure that she could have protein losing enteropathy related to this. She had no parasites. We have no evidence for collagen vascular disease. She could have an intestinal lymphoma that had metastasized to the kidney, and I think we should keep that in mind, although the evidence for that is very weak. If you look at signs and symptoms associated with diarrhea, looking at that question in a little bit different way, patients may present with arthritis (which she did not have). You can see ulcerative colitis, Crohn's disease, Whipple's disease, liver disease, liver malignancy or metastasis to the liver, fever, lymphoma, TB, ameba, ulcerative colitis, weight-loss, inflammatory bowel disease, cancer and malabsorption, eosinophilia she did not have, and lymphadenopathy. If in fact that was a lymph node in her chest it might make a primary lymphoma more likely. Whipple's disease and AIDS may have neuropathy - we don't have any evidence in the clinical presentation that she had neuropathy.

It could be associated with diabetic diarrhea or amyloidosis. She was not diabetic. The one thing that we notice is that she did have proteinuria and of course amyloidosis is associated with proteinuria.

If we look at amyloidosis and discuss classification of amyloid, it has changed over the years and is now basically a classification that is based on the subunit protein deposition in the tissues. Myeloma associated amyloid is called AL amyloid and now primary amyloidosis is the same disease. It involves deposition of kappa or lambda light chains as the amyloid protein. The other amyloid subtypes are all secondary to other disease processes and are classified by the subunit protein. We do not, in this patient, have serum protein or immunoprotein studies of the serum or urine to give us any evidence that there was a monoclonal protein present. In amyloidosis that is AL (primary amyloid), 80 to 85% of those patients will have a small protein spike that does not correspond to the diagnostic criteria needed to diagnose them as multiple myeloma patients. If you look at primary systemic amyloidosis, common syndromes that are associated with that diagnosis are carpal tunnel, peripheral autonomic neuropathy, renal disease which is by far and away the most common syndrome associated with primary amyloidosis and the most common manifestation of that is the nephrotic syndrome. A few of those patients will develop progressive renal failure. Cardiac amyloid is also a common problem with primary systemic amyloid and hepatic amyloid is present in about 15% of those patients, as well. It is a disease of aging because most of the individuals with monoclonal proteinureas are older, but can happen in a small percentage of individuals that are less than 40. If you look at the immunoglobulin monoclonal protein class, it is fairly obvious in primary systemic amyloidosis that lambda light chains are more toxic than kappa light chains as far as being nephrotoxic. There was an article in the *New England Journal of Medicine* that we reviewed in our Journal Club last month that brought a lot of discussion as to whether this is true. In the experimental model that was used, there was no difference in the renal toxicity of kappa chains and lambda chains.

I think that there are several potential diagnoses that could be entertained in this patient, but I think that her primary lesion is a renal lesion and my first choice would be that this was a renal cell carcinoma. She has nephrotic syndrome. She has a diarrheal syndrome that is best described as se-

cretory and she has hepatosplenomegaly so I think that the only way that I can tie all of those together is to give her systemic amyloidosis as well, associated with her renal tumor. It is said that between 3% and 5% of the patients with renal cell carcinoma will have amyloidosis associated with their tumor. The other thing that we should mention is that she had a rapid deterioration in her renal function and it is certainly possible that she had progressive renal vein or inferior vena cava thrombosis secondary to tumor extension into the vena cava.

In evaluating patients with renal cell masses the initial step is a renal ultrasound. CT scan can often be very helpful in defining whether there is extension into the inferior vena cava and is probably the next step to take. There were two procedures done in this patient. I would want to have histological diagnosis of what the primary lesion was and I would have biopsied the renal mass. Because she had nephrotic syndrome, I would have asked for a kidney biopsy at the same time. I'm not sure that's what was done, but that's probably what I would have done in that situation. The pathologist will now tell us what was done.

**Dr. Walker:** We received first the GI biopsy. Most notable is homogenous eosinophilic deposition that's acellular for the most part within the lamina propria. There is some deposition around vessels. This is homogenous eosinophilic material in otherwise fairly normal mucosa. This is a Congo red stain and you can see the intense red staining here in the lamina propria. This is consistent with amyloid deposition in a GI biopsy. Apple green birefringence from the amyloid stain under polarized light is specific for amyloid. In the final report, then, diagnosis was amyloid deposits in the lamina propria with a positive Congo red stain.

We received her left kidney. This was the gross specimen after the perinephric fat had been removed. You can see the large tumor mass in the lower pole here on the right, approximately 8 cm. The tumor extends into the renal vein. This is renal cell carcinoma. Microscopically, the glomeruli contained again some acellular homogenous eosinophilic staining material and for the most part in the mesangial areas. It does extend into some capillary loops. There's also staining outside the glomeruli around vessels and deposition in the interstitium of the kidney. Here again is polarized light on a Congo red stain specimen showing you apple green birefringence which is characteristic of amyloid. This is a Congo red stain showing amyloid deposition within and outside the glomeruli.



vessels. There is a lymphocytic infiltrate in that interstitium as well.

**Diagnosis:** Renal cell carcinoma  
Amyloidosis

2500 North State Street  
Jackson, MS

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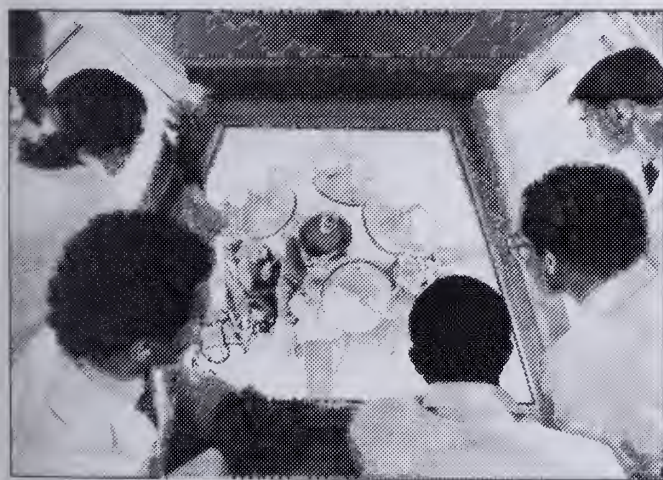
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*Dr. Files is Professor of Medicine and Associate Chairman for Clinical Affairs; Dr. Hamrick-Turner is Assistant Professor of Radiology; Dr. Walker is a Pathology Resident, all at the University of Mississippi Medical Center.*

*Dr. Adkins, Dr. Rees, and Dr. Simeone were Chief Medicine Residents in the Department of Medicine at the University of Mississippi Medical Center, 1991-92.*

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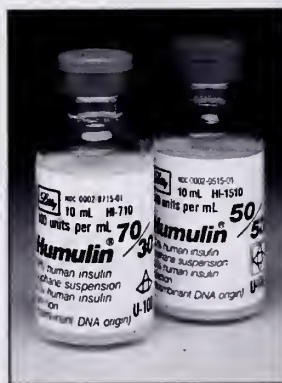
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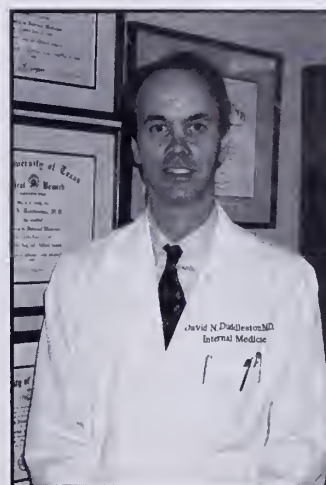
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# Hospice Care

David N. Duddleston, MD  
Linda Edwards

*The following interview with Dr. Duddleston was conducted and edited by Linda Edwards.*



Dr. Duddleston

***Your first referral to Hospice of Central Mississippi was in June of 1990. Why did you begin referring patients to hospice care?***

I had long seen the need for hospice care, and was very happy that Hospice of Central Mississippi was able to fulfill that need.

***What were your expectations concerning hospice care and were they met?***

I expected hospice care to provide total care for my patients and their families. Dealing with a terminally ill patient requires a knowledgeable, comprehensive, concentrative, and consistent kind of care that the hospice team approach provides. Yes, my expectations were met.

***What do you feel the benefits have been for your patients who have received hospice care?***

Well, I feel that in addition to what I have just said and perhaps of greater benefit to the patient, is to be given the opportunity to die with dignity at home, while not compromising in the actual care they receive. Hospice care also limits the financial burden on the patient and their family. While it is difficult for family members to care for terminally ill patients at home, they are benefited by the experience of caring for that loved one as that loved one may have cared for them in the past.

***What do you think are the reasons that some physicians have not considered hospice care as an option for their terminally ill patients?***

It's human nature to be afraid of death and suf-

fering, and at times it may seem easier to avoid considering hospice. However, medical professionals can overcome these traits by taking the time to evaluate the needs of their patient and the patient's family.

***Do you feel there is adequate communication regarding your patients from HOCM staff to you? Do you feel you have remained involved enough in the planning and directing of the care of your patients once HOCM receives the referral and begins caring for the patient?***

Yes, there is plenty of communication between the hospice staff and me. I have always felt I remained involved in the care of my patients and I am thankful that I am always given opportunity for input. The cellular phones your nurses have are a real plus. They give good access to your staff, perhaps that is why I have never had a problem contacting any staff member I needed.

***What is your initial consideration, when you refer a terminally ill patient to hospice care. What do you feel is the most important aspect of having your patient under hospice care?***

Again, I have to say it's the idea of total care of the patient and family being treated as a unit, with a whole team of hospice staff members available at their call.

***Recently you experienced hospice care in a way that most of our physicians have not, be-***

*ing involved personally. How did this experience affect the way you feel about the hospice philosophy of care?*

It was completely different to be on that end of hospice care, to have a family member die and to go through that experience was just a completely different aspect of hospice care for me. It is a challenge for anyone to be in the patient's family and to be part of the constant caring and support of that patient as well as to other family members.

Everyone in my family reacted differently and chose their own distinctive way of handling my mother's illness. We needed and got the extra support for family members as well as the actual physical care mother needed. Mother enjoyed the visits from the nurses and home health aids as much on a social level as on a professional level.

*Did you feel the hospice team (nurses, HHA's, social worker, bereavement counselor, chaplain and/or volunteers) visited your mother and dad enough to meet their needs? Did the extended family feel included?*

Yes, I feel their needs were met. Perhaps in retrospect, my father could have benefited from a better understanding of what to expect in the final moments of my mother's life, but in all fairness, one is never ready.

*As a physician what is your view on pain control? Was pain control an issue in the care of your mother? If so, did you feel it was controlled?*

On the issue of pain control, medicine has come a long way. Drugs for pain control are much better than they have been in years past and in just recent years there has been significant improvement in this area of patient care. Unfortunately for my mother, and due to extenuating health circumstances, we were not able to control her pain as well as we wanted. I will say, that the emphasis hospice places on pain management is great. Hospice of Central Mississippi nurses are quick to respond to the patients needs and get whatever is needed in the fastest manner possible. The hospice reputation in the area of pain management is accepted by physicians and they are eager to work with hospice care agencies because of that.

*I've noticed your referral pattern is to refer early in the last stages of illness. That is great, it gives us a chance to build trust with the patient/family and to prepare them for each new phase of the illness they will experience, as well*

*as to manage pain. However, even with your early referral, one patient elected not to use the program for a number of months after the initial request was made. Once a referral is made, what can HOCM do to affect patient acceptance?*

Sadly, in some cases, that is true. Initially, the physician can help by encouraging the family to accept hospice care earlier. Perhaps families see hospice care as a service only, rather than a philosophy of care and they wait until the situation is at the crisis level before they are willing to enroll. Some may even view it as giving up hope. My suggestion would be to evaluate as soon as a referral is made and encourage the family to let the patient make the decision based upon all the options that are available. Many times if the family finds out what the patient's wishes are, it makes it easier for all to accept the illness and prepares them to accept the help hospice is ready to give.

*Because of your complete hospice experience, what message would you send to physicians who haven't considered using the hospice philosophy of care, or who only refer occasionally?*

My message would be to refer early. Whenever a terminal illness is diagnosed, that is the time to start talking about hospice. Giving all the options early in the final stages allows the patient the opportunity to make decisions based on their own wishes and desires for quality of life. □

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*Dr. Duddleston is in the practice of internal medicine, 1190 N. State Street, Bldg, 201, Jackson and Ms. Edwards is Education Coordinator, Hospice of Central Mississippi, Inc., Jackson.*

*For further information on hospice care contact the Hospice Care Organization nearest you or Hospice of Central Mississippi, PO Box 12486, Jackson, MS 39216-4911, 366-9881 • 1-800-273-7724.*



# IMPORTANT NOTICE

## New Charitable Immunity Law to Take Effect on July 1

In the recently completed 1993 Legislative Session, MSMA successfully secured enactment of a law which grants immunity from liability to physicians who voluntarily provide care without the expectation of payment due to the person's inability to pay for the services.

There are some important factors that need to be kept in mind by the physician and his/her staff if they want to take advantage of the immunity available under this new law. Therefore, please remember the following:

1. The immunity applies only to those patient encounters occurring on and after July 1, 1993. It cannot be applied to any care prior to that date even if the physician elects to waive collection of any past-due payments which existed before July 1.
2. The immunity will apply only in those situations where the physician VOLUNTARILY elects to provide care without expecting to be paid for the services. The law does not apply to care of an emergency nature, or any other situation in which the physician is legally or ethically required to provide care.
3. The Physician's willingness to provide services without being paid and the patient's understanding that they are waiving their right to pursue legal action **MUST** be evidenced in writing and signed by both the physician and patient. A **SAMPLE AGREEMENT WHICH YOU MAY DUPLICATE AND USE FOR THIS PURPOSE IS ON THE BACK OF THIS PAGE.**
4. The immunity will not be granted in those situations where the patient has the means or resources to pay for the services.
5. No bill or statement of charges should be sent to a patient for whom this law would apply and who has signed the agreement mentioned above. Sending a bill or other statement might be an indication that the physician expected to be paid and there must be no expectation of payment in order for the immunity to apply.
6. The immunity afforded under this law is not applicable to situations involving willful or gross negligence.

Please contact the MSMA office if you have any questions about the charitable immunity law.

**AGREEMENT TO PROVIDE CARE WITHOUT COMPENSATION  
AND WAIVER OF LIABILITY**

WHEREAS, \_\_\_\_\_ (physician), voluntarily agrees to provide necessary medical care and services to \_\_\_\_\_ (patient) without expecting to be compensated for those services due to the patient's inability to pay for the services.

WHEREAS, patient desires to have the professional medical services provided by physician, but is unable to pay for those services and is willing to waive his/her right to take legal action against the physician for negligence that is not of either a willful or gross nature.

NOW, THEREFORE, BE IT RESOLVED, that physician and patient agree that:

1.) The physician will voluntarily provide necessary medical care and services to the patient without expecting the patient to pay for those services and no attempt will be made to collect any payment for those services. This agreement applies to all services rendered by the physician from and after the date of this agreement and it shall remain in effect until terminated by the physician on the date indicated below.

2.) The patient understands that he/she will not be charged for services provided by the physician and in consideration of receiving the services free of charge the patient further understands that under Mississippi law he/she is prohibited from taking legal action against the physician for any injuries resulting from treatment that are not due to willful or gross negligence.

AGREED TO this \_\_\_\_ day of \_\_\_\_\_, 199\_\_.

\_\_\_\_\_  
Signature of Physician

\_\_\_\_\_  
Signature of Patient (parent or guardian  
if patient is a minor)

This Agreement was voluntarily terminated by the physician on \_\_\_\_\_.  
(This should only be completed and signed by the physician if the Agreement is terminated.)

\_\_\_\_\_  
Physician

THIS AGREEMENT SHOULD BE KEPT IN THE PATIENT'S MEDICAL RECORD.



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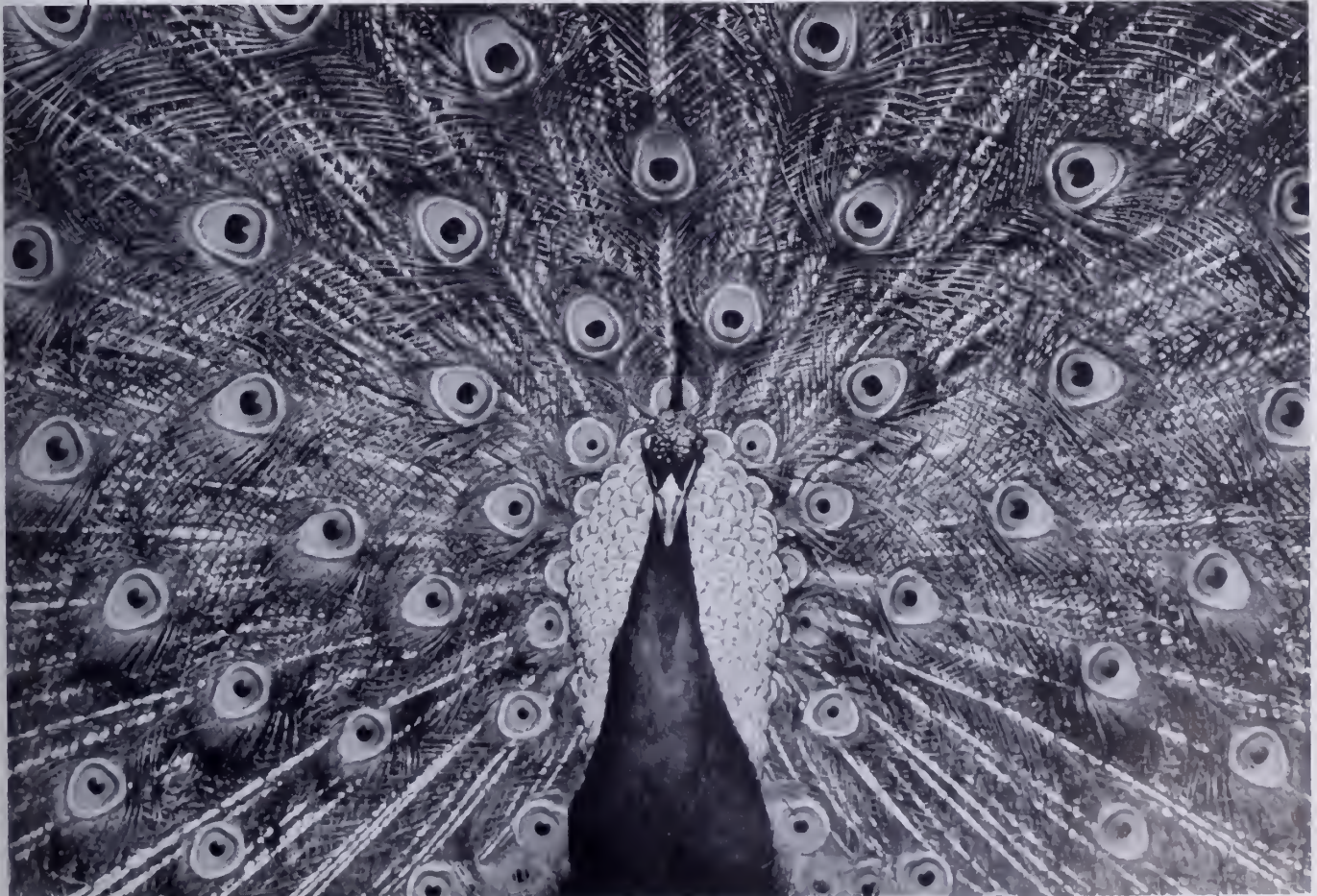
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## The President's Page

DON Q. MITCHELL, MD

### "The Devil Is In The Details"

**I** have just returned from our AMA Annual Meeting. It was long! It was tiring! It was simulating! More than 430 delegates participated in the five day session.

By now you have all heard that Mrs. Hillary Rodham Clinton, the First Lady, addressed the opening session of our House of Delegates. A polished and persuasive speaker, she said just what we wanted to hear regarding the issues of reform.

All of the major points Mrs. Clinton made regarding "health care reform" are those included in Health Access America and Health Access Mississippi that we have been talking about for the past three years. Some of the issues she addressed were: access to care, cost containment, ensuring and enhancing quality of care and maintaining the patient's right to choose a physician.

Mrs. Clinton began by saying, "We must guarantee all Americans access to a comprehensive package of benefits no matter where they work, where they live, or whether they have ever been sick before." "Secondly, we do have to control costs." I think we can all agree with both of these statements but we need to know how this will be accomplished and most importantly at what cost. In this reform plan the **"devil is surely going to be in all the details."**

Mrs. Clinton also said, "One thing we can all agree on is that we have to cut down on the paperwork and reduce the bureaucracy in both the public and private sector." We strongly agree. She cited examples with which we are all familiar. One of these was that the typical doctor's office, now spends 80 hours a month on administration with part of this time spent filling out duplicate forms for government agencies and insurance companies. She also questioned, just as we do, "how a person with little or no medical knowledge sitting at a computer, thousands of miles away, can make a judgement about what should or shouldn't happen at a patient's bedside."

"Let us remove the kind of micro-management and regulations that have not improved quality and have wasted billions of dollars," Mrs Clinton said. "We

*(Continued on page 240)*



## You Know the Plan Is In Trouble When She Comes to the AMA

The newspaper articles are still scattered about on my table. I've just switched off the evening television news. Mrs. Clinton has at last spoken to the AMA about health care reform. She was all conciliation in Chicago. For our troubles, she said, the insurers, along with government agencies, were to blame for second guessing medical decisions. And, of course, the system itself was to blame for providing us doctors with perverse rewards for "over-prescribing, over-testing and generally overdoing." She won repeated applause for promises of relief from antitrust laws and onerous laboratory regulations.

But wasn't it only a few weeks ago that, speaking before a union, she blamed the "price-gouging" and "profiteering" medical establishment for opposing any meaningful health care reform? And wasn't it only February when she excluded the AMA and experienced practicing physicians in general from a role in developing a new health care system?

Take this speech to the AMA for what it is, a sign of weakness. In February, with public opinion on her side, she could afford to look the other way. She chose to exclude us in hopes of a quick victory. Now in June she comes to the AMA looking for support, just as reason said all along she would have to, either before the plan

was enacted or after it was in shambles.

Even now, however, she offers not a seat at the planning table, but only a handful of promises and no information, none whatsoever, about global budgets, rationing, and what role the practicing physician will have in telling patients they can't have what they might want or need. But this, too, will change. Her ship of health care reform is drifting steadily toward the rocks of employer resistance to high payroll taxes and citizen's reluctance to be told from what list to choose their doctor. Even Democratic congressional leaders now say the outlook for passage of a plan in 1993 is dim. Passage next year might be even more unlikely given it will be an election year coming on the heels of major tax increases.

There will come a time when Mrs. Clinton's offensive, so powerful in February, will have shot its bolt. Then, in order to get something, anything, passed, she will speak to us more seriously, not just from a lectern but from across a table. The AMA has formulated proposals for health care reform that deserve a serious discussion. And that will come. Bet on it.

**Leslie E. England, MD**  
Associate Editor

The editorial opinions expressed in this Journal are those of the indicated author. Editorial opinions are not expressions of the views, or official policies of The Mississippi State Medical Association. We encourage the membership to submit letters for publication regarding any opinion expressed or information contained in the Journal.

## President's Page

(Continued from page 238)

have to simplify and eliminate the burden from regulation created under CLIA ... a well-intentioned law with many unexpected consequences." She also said, "we will offer a serious proposal to curb malpractice problems."

Regarding choice the First Lady said, "we have also, very much, put choice in the center of our system -- so that we will have not just choice for patients

as to which plan they choose to join, but choice for physicians as to which plan they choose to practice with -- including the option of being part of more than one plan at the same time."


As I mentioned at the beginning, Mrs. Clinton very eloquently said everything she knew we wanted to hear, but I, as well as you, know that it will be those "devilish details" that affect how you and I practice medicine.

It was obvious to me as I

listened to Mrs. Clinton speak that she has discussed and reviewed each issue with a practicing physician. She described our concerns almost too precisely, yet I know she has heard our views. What the outcome will be I don't know.

Like everyone else, we will just have to wait and see.

Your colleague,



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## LETTERS

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June 9, 1993

### Board of Trustees Mississippi State Medical Association

Dear Friends and Colleagues,

Memory of my first affiliation with the Mississippi State Medical Association is quite vivid and dates back to 1957.

I had entered practice in Pickens in 1957. The Mississippi State Medical Association leaders in Holmes County were Paul Brumby, and Arthur Derrick; they each contacted me shortly after I had hung out my shingle and welcomed me to Holmes County and extended an invitation to join North Central Medical Society and the Mississippi State Medical Association. A few weeks later, perhaps in September, Dr.

Brumby reminded me that I should attend the next meeting of the North Central and gave me an application for membership.

I remember going to the meeting with Dan Mitchell and several others where I submitted my application for membership.

Membership and the opportunity to participate in Mississippi State Medical Association have been important parts of my professional career in public health here in Mississippi.

On many occasions, I turned to Mississippi State Medical Association for guidance and support. The most significant measure of support came during the Cliff Finch Administration. Governor Finch and members of his staff made an attempt to take political control of the State Department of

Health.

The Mississippi State Medical Association provided the support including legal which made the critical difference in the preservation of the department as a public health physician directed agency.

It is therefore, with a special sense of pride and gratitude, that I receive the Resolution of Service Appreciation which the Mississippi State Medical Association Board of Trustees presented to me at our last annual session.

Our association and its physician leaders and its administrative staff will always hold a very special place in my professional and personal memory. Thanks for everything.

Sincerely,

Alton B. Cobb, MD, MPH  
Principal Clinical  
Coordinator



## **BILOXI MSMA 1993: A MEETING IN REVIEW**

The Royal d' Iberville Hotel, 6:00 a.m. - Sunday: I was jolted awake by what I thought was my heart pounding wildly and erratically out of my chest. A brief reality check revealed the actual source to be a "boom-box" whumping away at an early morning party in the next room.

"Kah-chung-gah, Kah-chung-gah, Boom, Boom, Boom....Kah-chung-gah... ad infinitum", you get the idea, Primordium emanating from a mega-woofer.

We've all encountered cars equipped with these boom-boxes on the street. These are only tolerable because they come and go with relative rapidity. But the people in 605 were the same folks the FBI hired to drive David Koresh wacko out in WACO. They were just passing through Biloxi on their way back home.

I let my bone marrow resonate for about 10 minutes before I called the front desk. An extremely sympathetic young man promised he would take care of it right away and, by George, in 5 minutes all was quiet. Those people in the next room actually came by later and apologized for their "carelessness and insensitivity."

This event and their response somehow typified our whole stay at the Royal d'Iberville. The service was fast and the employees were uni-

formly helpful and friendly. I asked for extra towels a time or two and actually got them (without a hassle) less than 10 minutes later.

One criticism though, the owners should really renovate the rooms. Ours had that same old stained and really nappy green carpet that it had 10 years ago. This in combination with high humidity made our room smell like a delightful combination of yesterday's sweat socks and last week's "catch-of-the-day".

The physical aspects aside, our 1993 annual MSMA meeting was most enjoyable. The generally uncooperative weather gave us a good excuse to keep the kids out of the water (for the most part) and we even got to see and do some enlightening things around the area . . . the J. L. Scott Marine Aquarium, the Walter Anderson Museum, the Shearwater Pottery, and the neat little shops in Ocean Springs. We even discovered the clean Gulf State Park where our boys could wet a hook from a covered pier.

Biloxi is less depressing now that it has been resuscitated. Those boarded up store fronts and "ghost motels" on Highway 90 are beginning to disappear. Even the beaches seem cleaner. Someone must have finally decided that broken beer bottles and dead fish don't make for an appealing day at the beach.

Hard as I try, though, I just can't love all that gambling

mess. Mississippi River Paddle wheelers just seem so gaudy and out of place parked in the Gulf of Mexico. Hopefully, the economic boom they are feeling on the coast isn't a pyrrhic victory. I'm afraid that a lot of the money lost in the casinos may come from folks on the coast who can least afford to lose it. I hope I'm wrong.

Attendance at this year's meeting was down a bit, only 219 physicians were registered. Frankly, I expected a crowd what with all the changes likely to soon take place in the lives of all us medical folk. I was anxious to talk to fellow MSMA members to see if anyone had a feel for what's going to happen to us and how best to deal with it.

As it turned out, we were all pretty much in the dark, but somehow it's relieving to find out that you're not really alone. Being in solo practice you tend to become rather isolated. I spend my days talking almost exclusively to patients and my nights trying to make it up to my children for not spending more time with them. Sometimes you just get kind of ground down.

When I attend these meetings it's just great to see everybody that we've come to know there from years' past. It's so helpful to talk to folks that have some of the same problems and concerns that I do.

Participating in the Reference Committee meetings and House sessions is entertaining

and quite stimulating. It beats the heck out of those loathsome discussions on cephalosporins and calcium-channel blockers

I wish more people on a statewide level would wake up and get involved, especially more of the women physicians. I've heard a few people say that MSMA is a "good ole Boys' Club." Well, that is simply not true. The vast majority of the guys who are active in MSMA go out of their way to encourage women to take active roles and assume positions of leadership.

The State Medical Meeting feels almost like a family reunion to me now. There's always an abundance of good food and good fellowship but especially, good folks. And I'm thankful for the opportunity to be among their ranks.

Dwalia S. South, M.D.  
Family Practice,  
Ripley, MS

## Medical Terminology Course

A seminar entitled *Introduction to Medical Terminology* and sponsored by Central Chapter Medical Assistants will be held, Friday, July 23, 1993 at the School of Nursing Auditorium, University Medical Center, Jackson. This one day course is approved for 0.6 AAMA-CEUs. For further information contact: Pamela K. Fryer, CMA, workshop coordinator, 984-5330.

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## Dr. Stockton Honored for Health, Welfare Ministry

Dr. Wendell Stockton, an Amory pediatrician, was recently named Health and Welfare Leader of the Year 1993 by the United Methodist Board of Global Ministries.

Dr. Stockton was chosen to receive the award after a decade of service to the Mississippi Conference Committee on Health and Welfare Ministries, which he has chaired for the past eight years. This committee consisting of about 30 people oversees all Methodist health and welfare services in Mississippi and deals with services running the gamut from senior services to children's programs.

The Rev. Warren C. Black, pastor of St. Andrews United Methodist Church in Amory, Stockton's home church, said of the doctor's award, "This is an outstanding honor for many years of his dedicated and faithful service to the health and welfare ministry of our church."

Dr. Stockton, a charter member of the St. Andrew's church, donated the land for the church when it was established in 1960. He is a member of the choir and a Sunday School Teacher.

His ministry, however, does not stop at the church door. He

has founded numerous ministries through his profession. Since 1949, Stockton has practiced pediatric medicine in Amory, where he established the first neonatology program in the state. In 1970, Dr. Stockton initiated a local program for mentally handicapped children which served as a model for others across the state. Dr. Stockton and his wife Nancy, led in the efforts to create a "Meals on Wheels" program in their community. With Mrs. Stockton's leadership and Dr. Stockton's support, this program has been on-going since 1972 using volunteers and mostly local funding.

Dr. Stockton has served at various times on the boards of directors/trustees of United Methodist Senior Services of Mississippi, Inc. United Methodist Children's Home, Methodist Health Systems, and Rust College, as well as numerous conference and general agencies of the church. Stockton also serves on the state legislative committee for pediatrics and infant mortality. He is commissioner of mental health for Region III and he serves on the state Committee for Maternal Mortality.

His latest project is a "parish nurse" program, a model of

which he has instituted at St. Andrews. Utilizing nurses, doctors and other medical personnel within the congregation, the parish nurse program makes a nurse available to the community for blood pressure, blood sugar and cholesterol checks. At St. Andrews, members of the parish nurse program are set up for checkups at the church on Sunday mornings. They also check medications to look for duplication or medicines that could interact.

"I hope we can set up this program all over the state," Dr. Stockton said in a recent interview at his clinic.

As for his next project, he said he doesn't know yet what it is, but one thing's for sure: He has no plans to retire either from his practice or his ministry. It is his desire to help other than makes life worth living, he said. □



### Kirk Mullins of Natchez Receives Evers and Tolbert Awards

Walter Kirk Mullins of Natchez, third from right, was among medical students recognized for academic achievement during School of Medicine honors day ceremonies at the University of Mississippi Medical Center in Jackson. Mullins, the son of Mr. and Mrs. James P. Mullins, received the Carl Gustav Evers award and Virginia Stancil Tolbert award. The

Evers award, established this year by the Mississippi State Medical Association Foundation to honor the late Dr. Carl Evers, associate medical school dean for academic affairs, and a long-time active member of the Mississippi State Medical Association, is given for scholarship, peer support, and exceptional leadership in student activities of the American Medical Association.

tion and the state medical association. Dr. Evers' daughters Julie, second left, and Karen, second right, and his widow Jan, third left, were present for the ceremony. The Tolbert award is given for scholarship and leadership. Dr. Norman C. Nelson, left, is UMC vice chancellor. Dr. Lincoln Arceneaux, right, is medical school associate dean for student affairs. □

### Dr. McDonald Guest Lecturer

Dr. John C. McDonald was guest lecturer at Amite-Wilkinson Medical Society and Field Memorial Community Hospital's 15th annual lectureship. He spoke on the topic, *A Mississippian's Journey Into Organ Transplantation*.

Dr. McDonald is Professor and Chairman, Department of Surgery, Louisiana State University School of Medicine in Shreveport. He was born in Baldwin, Mississippi and holds a BS degree from Mississippi College and an MD degree from Tulane University School of Medicine in New Orleans. He is currently the Surgeon in Chief, LSU Medical Center, Shreveport, and

Director of Louisiana Organ Procurement Agency. He is a founding member of the American Society of Transplant Surgeons and presently serves as a member of the Southeastern Surgical Congress and Southern Surgical Association. He has served as president of both the American Society of Transplant Surgeons, and United Network for Organ Sharing. □



## Dr. Hollis Serves As President Of The American College of Obstetricians and Gynecologists

Dr. Richard Hollis, a practicing Ob/Gyn in Amory for 35 years assumed the top position within the American College of Obstetricians and Gynecologists (ACOG), at the group's 41st annual clinical meeting in Washington, DC.

Dr. Hollis has a long record of service to ACOG, having been a active member of the organization at the state and national levels. He has been president elect for the past year and previously served as an elected officer for the Mississippi section and for his district.

Dr. Hollis said at the time he was named president elect that several issues would be top concerns in the medical profession in coming years, including ac-

cess to health care, quality of health care and cost containment.

These same concerns have since been included in the discussions of a national health-care program expected to be unveiled next month.

Dr. Hollis, a Amory native, is affiliated with Gilmore Memorial Hospital in Amory where he has maintained a major administrative commitment. He currently serves on numerous committees including the Ob/Gyn and Surgery Committee, and is former chief of Ob/Gyn Services.

He is clinical associate professor of Ob/Gyn at the University of Mississippi Medical School, adjunct clinical professor for Mississippi University for Women, and is one of the

founders of the Physicians and Surgeons Clinic in Amory.

He received his medical degree for the Tulane School of Medicine in New Orleans.

Last year, Dr. Hollis was presented with ACOG's Outstanding District Service Award for the contributions and leadership he has provided to his district while promoting the ideals of the college. His commitment to the education of members with the goal of improving the quality of women's health care was especially recognized.

He has been president of the Mississippi State Ob/Gyn Society, Conrad Collins Tulane Ob/Gyn Society and the Northeast Mississippi Medical Society. □

## Dr. Fenter Receives First A. A. Derrick Memorial Award

Dr. Thomas C. Fenter of Jackson, right, receives the **A. A. Derrick Memorial Award** from Dr. Richard Miller, chairman of the Mississippi Foundation for Medical Care (MFMC) board of directors. The award was presented by the MFMC board in memory of Dr. Arthur A. Derrick of Durant, a former chairman of the MFMC board, for his support of the peer review organization over the years.

Dr. Fenter has been active with MFMC since 1977 in various capacities, including associate medical director, speakers bureau chairman, review physician and criteria advisor. □



## 1993 Caldwell Award Winner

Gary L. Smith, MD, left, was presented the 1993 Robert S. Caldwell Memorial Award by R. Faser Triplett, MD, right, during ceremonies at the MSMA Annual Session. Dr. Smith was selected by an ad hoc committee of UMC faculty, in recognition of in-training excellence in medical practice, patient relations, and documentation of patient care. A native of Meridian, Dr. Smith received his BS and MD Degrees from the University of Mississippi. After completing his residency training in May, Dr. Smith and his wife, the former Nancy Gillespie, will remain in Jackson where he will join the UMC Anesthesiology Department as a Teaching Assistant.



The Caldwell Award, presented each year by the Medical Assurance Company in the interest of furthering medical-legal education, is given in memory of the late general surgeon from Tupelo. Dr. Caldwell was instrumental in mustering initial support for and participation in the Company. He served on MACM's first Board of Directors and was elected the Company's first Secretary. □

## Medical Society Gives Local Students Awards for Academic Excellence

The Singing River Medical Society (composed of 92 Jackson County Physicians) established the Singing River Medical Society Award of Achievement in 1991 to recognize and award excellence in language/communication skills (based on English ACT scores) as demonstrated by a graduating senior at each of the seven high schools in Jackson County. The 1993 recipients are as follows:

Carrie Larue - St. Martin High School - daughter of Mr. & Mrs. Bill Larue, English ACT score 36 - plans to attend Texas A & M University; Jessica Janus - Ocean Springs High School - daughter of Mr. & Mrs. Gene Janus - English ACT Score 33 - plans to attend the U.S. Naval Academy; Crystal Johnson - Moss Point High School - daughter of Glenda Noble - English ACT Score 32 - plans to attend Tulane University; Trisha Wages - Vancleave High School - daughter of Mr. & Mrs. Jerry Wages - English ACT score 32 - plans to attend the University of Southern Mississippi; Susan Ann McCloskey - Pascagoula High School - daughter of Dr. & Mrs. John McCloskey - English ACT score 31 - plans to attend Emory or Duke University; Casey Pedersen - East Central High School - daughter of Mr. & Mrs. Allen Pedersen - English ACT score 29 - plans to attend the University of Mississippi; and Chris Hiestand - Resurrection Catholic High School - son of Edward Hiestand English ACT score 26 - plans to attend Mississippi State University. □

## Dr. Field Installed as Surgical Congress President



Richard J. Field, Jr, MD of the Field Clinic and Field Hospital of Centreville was installed as President of the Southeastern Surgical Congress in Tarpon Springs, Florida, on February 10, 1993. The Southeastern Surgical Congress is composed of 3,500 surgeons predominantly

from the southeastern United States and is the 2nd largest surgical organization in the United States. He has previously served as vice president and councillor during the past ten years. □





**Frank Morgan, MD, Receives John H. Clark Leadership Award**

## **Executive Officer Recipient of Federation Award**

The Mississippi State Board of Medical Licensure's, Executive Officer, Frank J. Morgan, Jr., MD, MPH, was recently honored with a prestigious award at the Federation of State Medical Boards' annual meeting in San Francisco, California on April 24, 1993.

The award known as the "Dr. John H. Clark Leadership Award" is presented annually by the Federation to an individual exhibiting qualities consistent with the goals and directions of the Federation of State Medical Boards of the United States.

The award states "In recognition of his distinguished leadership in the field of Medical Licensure and Discipline. His dedicated efforts in state and national efforts to further the goals of the Federation of state Medical Boards and advance the public good and the spirit of service exemplified by John H. Clark, MD, 61st President of the Federation.

Dr. Morgan has been actively involved with medical licensure for 20 years. He first served as the assistant secretary for the Mississippi State Board of Medical Licensure then as the assistant state health officer for licensure and certification. In 1980 he became the executive officer of the Mississippi State Board of

Medical Licensure, his current position.

Dr. Morgan has been active in the Federation of State Medical Boards for over 15 years serving on the FLEX Test Committee, the Bylaws Committee, the Resolutions Committee, and several special ad hoc committees. He has served on the Federation's Flex Board, now the Examination Board, for 11 years, and is currently serving as the Board's chairman.

He was appointed a member of the USMLE Composite Committee in 1991. Dr. Morgan has just recently been appointed a Federation Representative to the National Board of Medical Examiners. □

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# The University of Mississippi Medical Center

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## Greenwood Resident Named Top Graduate

Bryant Wolfe Lary of Greenwood (right center) received the **Virginia Stancil Tolbert Award** at the University of Mississippi Medical Center Commencement in Jackson. The award, sponsored by the Mississippi State Medical Association, goes to the graduating senior in the UMC School of Health Related Professions who has the highest academic average. Lary earned his B.S. degree in physical therapy. He is the son of Mr. and Mrs. W. L. Lary, Jr. of Greenwood.

Commencement participants include (from left) Dr. R. Gerald Turner, chancellor of the University of Mississippi; Dr. J. Maurice Mahan, dean of the UMC School of Health Related Professions; Lary; and Dr. Norman C. Nelson, UMC vice chancellor for health affairs. □



## Drs. Roberts and Morrison Present Results of Study

Dr. William E. Roberts and Dr. John Morrison of the University of Mississippi Medical Center found in a five-year study that through early diagnosis and aggressive drug treatment, 76 percent of women medically at risk to deliver early can carry their babies to term.

They presented their findings at the annual meeting of the American College of Obstetricians and Gynecologists in Washington recently.

Previous studies of such patients found 25 percent carried their babies to term, the physicians said. The UMC study excluded women who must deliver early to save themselves or their infants.

"We think it's extremely significant because pre-term labor is the leading cause of preventable infant mortality," said Dr. Morrison, professor of obstetrics and gynecology at UMC. "No. 2, it's very common — 250,000

to 300,000 women have pre-term babies a year. We can reduce the number."

The 17,186 at-risk patients constituted the largest patient population studied for pregnancy outcomes. Most studies dealing with such risk factors look at 350 to 400 patients. The UMC study drew patients nationwide through a computer data base to show that the system is as effective in New York and in Mississippi, Dr. Morrison said. □



## Dr. John H. Eichhorn Receives Merck and Company Health Award

Dr. John H. Eichhorn, chairman of anesthesiology at UMC, received the 1993 Merck and Company Award for Advances in Health Care Quality sponsored by the American College of Physician Executives.

He received the national recognition for creating safety standards in anesthesia practice which have now been adopted worldwide.

Dr. Eichhorn proposed the standards at Harvard Medical School in 1985 after a review of catastrophic anesthesia accidents showed the most fell in the

"preventable" category.

In 1980, the rate of catastrophic anesthesia accidents nationwide was about one in 10,000 to one in 20,000. After standards were adopted at Harvard, the rate of such accidents there decreased to one in 392,000. □

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## New Members

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**Casano, Peter J., IV**, Jackson. Born New Orleans, LA, April 3, 1962; MD, University of Mississippi School of Medicine, Jackson, MS, 1988; interned and otolaryngology & neck surgery residency University Medical Center, Jackson, MS, 1988-93; elected by Central Medical Society.

**Feldberg, Murray S.**, Greenwood. Born New York City, NY, August 28, 1931; MD, Fac. of Medicine, University of Amsterdam, the Netherlands 1957; interned one year Fordham Hospital, Bronx, New York; psychiatry residency, Vanderbilt University Hospital, Nashville, TN, 1960-62; fellowship child psychiatry, Children's Hospital, Washington, DC, 1962-64; elected by Delta Medical Society.

**Kanosky, Michael Glenn**, Jackson. Born Greensburg, PA, February 1, 1960; MD, Louisiana State University School of Medicine, New Orleans, LA, 1986; interned and surgery residency Charity Hospital, New Orleans, LA, 1986-90; fellowship in plastic and reconstructive surgery, University Medical Center, Jackson, MS, 1991-93; elected by Central Medical Society.

**Mallette, Presley D.**, Pascagoula. Born Biloxi, MS, October 4, 1962; MD, University of Mississippi School of Medicine, Jackson, MS, 1988; interned and anesthesiology residency, University of Texas Medical Branch, Galveston, TX, 1988-92;

elected by Singing River Medical Society.

**Newell, Ronald B.**, Greenwood. Born Meridian, MS, January 20, 1946; MD, University of Mississippi School of Medicine, Jackson, MS, 1972; interned and general surgery residency, Lloyd Noland Hospital, Fairfield, AL, 1972-74; orthopaedic surgery residency, University of Alabama Hospital, Birmingham, AL, 1974-77; elected by Delta Medical Society.

**Nicholas, Lawrence M.**, Yazoo City. Born Yazoo City, MS, June 13, 1943; MD, Tulane University School of Medicine, New Orleans, LA, 1968; interned one year, Baptist Memorial Hospital, Memphis, TN; general surgery residency, University of Alabama Hospital, Birmingham, AL, 1969-73; thoracic & cardiovascular surgery residency, University of Tennessee, Memphis, TN, 1978-80; elected by Delta Medical Society.

**Rogers, Clifton**, Byhalia. Born Memphis, TN, June 1, 1955; MD, Meharry Medical College School of Medicine, Nashville, TN, 1982; interned Hubbard Hospital for one year; family practice residency, St. Mary's Hospital 1983-85; elected by North Mississippi Medical Society.

**Ryan, Hewitt Fitts**, Columbus. Born Albion, NY, November 17, 1928; MD, University of Rochester School of Medicine, Rochester, NY, 1958; interned one

year University of Chicago Clinics, Chicago, IL; psychiatry residency, University of Colorado Medical Center, Denver, CO, 1959-62; elected by Prairie Medical Society.

**Stanford, J. Keith**, Grenada. Born Jackson, MS February 1, 1962; MD, University of Mississippi School of Medicine, Jackson, MS, 1989; interned and family medicine residency, University Medical Center, Jackson, MS, 1989-92; elected by North Central Medical Society.

**Vaughn, Cynthia Ann**, Jackson. Born Greenville, MS, August 25, 1951; MD, University of Mississippi School of Medicine, Jackson, MS, 1978; interned and family medicine residency, University Medical Center, Jackson, MS, 1988-89; anesthesiology residency, same, 1990-93; elected by Central Medical Society.

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## Deaths

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**Stephenson, Samuel L.**, Jackson, MS. Born Marks, MS, July 3, 1914; MD, University of Tennessee School of Medicine, Memphis, TN, 1936; interned one year Lloyd-Noland Hospital, Birmingham, AL; medicine residency, Kennedy Hospital, Memphis, TN, 1947-49; gastroenterology residency, same, 1949-52; died May 5, 1993, age 78.

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**Tim Alford** of Kosciusko has been elected to the Mississippi Foundation for Medical Care board of directors to serve through 1995.

**Paul M. Allen**, a gynecologist and obstetrician practicing in Pascagoula, gave a presentation entitled, *Risk Management Issues in the Physician's Office* during the 13th Educational Conference of the Southern California Association of Healthcare Risk Managers in California on May 13.

**William Arnett** of Hattiesburg has been elected to the Mississippi Foundation for Medical Care board of directors to serve through 1995.

**Oscar Briseno**, a general surgeon from Union, recently attended an Advanced Laparoscopic Seminar at the CMC Medical Training Center located in Nashville.

**Luis V. Borrell** has associated with The Medical Group, 305 South Archusa Avenue, Quitman, in the practice of pulmonary and internal medicine.

**Rick Carlton** of Jackson has been installed as president of the Mississippi Chapter of Emergency Physicians.

**Linda Chidester** of Mantachie has been granted membership in the Southern Medical Association.

**John Cook** of Jackson has been selected to serve as president-elect of the Mississippi Chapter of Emergency Physicians. He has been elected to the Mississippi Foundation for Medical Care board of directors to serve through 1995.

**Ralph Daniel, III**, of Jackson was recently visiting professor at the University of Virginia for two days discussing nail and fungal disorders of the skin.

**Jack Evans** of Laurel has been elected to the Mississippi Foundation for Medical Care board of directors to serve through 1995.

**Larry Field** and **Buddy Savoie** of Jackson presented a scientific paper entitled *Arthroscopic Repair of Superior Labral Detachment Lesions of the Shoulder: Techniques and Clinical Results* at the Specialty Day, American Academy of Orthopaedic Surgeons Annual Meeting.

**Carolyn Gerald** of Brookhaven has been elected to the Mississippi Foundation for Medical Care board of directors to serve through 1995.

**William Henderson** of Oxford has been elected to the Mississippi Foundation for Medical Care board of directors to serve through 1995.

**William G. Jackson**, a family practice physician in Corinth has been elected to the advisory board of Deposit Guaranty Na-

tional Bank-Corinth.

**Dan W. Jackson**, a family practice physician from Rolling Fork, recently attended the symposium *Third Annual Focus on the Athletic Patients* sponsored by SMA.

**Scott Jones** and **Buddy Savoie** of Jackson presented at Specialty Day, American Academy of Orthopaedic Surgeons Annual Meeting, a scientific paper on *Release of Flexion Contractures of the Elbow*.

**Chester H. Lake, Jr.**, has associated with Surgicare of Jackson as Medical Director and anesthesiologist.

**William A. Middleton**, a family practice physician of Winona and member of the MSMA Council on Legislation, received the annual award of *Outstanding Contributions to Montgomery County* in the area of government and professional groups for the year 1992-93 during the Montgomery County Economic Council annual banquet.

**Tom Montgomery** and **F. H. Savoie** presented a scientific paper entitled *Comparison of Arthroscopic Debridement versus Open Full Thickness Rotator Cuff Repair* at the Specialty Day, American Academy of Orthopaedic Surgeons Annual Meeting.

**Francis Morrison** of Jackson has been elected to the Mississippi Foundation for Medical

Care board of directors to serve through 1995.

**Morris Parsons**, of Ackerman has associated with North Mississippi Family Medical Clinics, Inc., 119 West Cherry Street, Ackerman.

**Sam Peebles** of Jackson has been elected to the Mississippi Foundation for Medical Care board of directors to serve through 1995.

**Hildon H. Sessums, Jr.**, of Vicksburg, has been accepted as a member of the Mid South Occupational and Environmental Medical Association, the regional organization affiliated with the American College of Occupational and Environmental Medicine.

**Max Taylor** of Tupelo has been elected to the Mississippi Foundation for Medical Care board of directors to serve through 1995.

**Billy Walker**, a dermatopa-thologist in Jackson received a Masters of Business Administration degree during the Millsaps College Graduation exercises, May 8, 1993. He was also inducted into Beta Gamma Sigma, the National Business School Honorary for Academic Achievement.

**Jimmy Walker** of Jackson has been elected to the Mississippi Foundation for Medical Care board of directors to serve through 1995.

**Stevan A. Webster**, has associated with Internal Medicine Clinic of Laurel, in the practice of cardiology.

**Peggy J. Wells**, a pediatrician of the Children's Clinic of Clarksdale, was voted 1993 Doctor of the Year by employees of the Northwest Mississippi Regional Medical Center. □

## Send Items for the Personals Column

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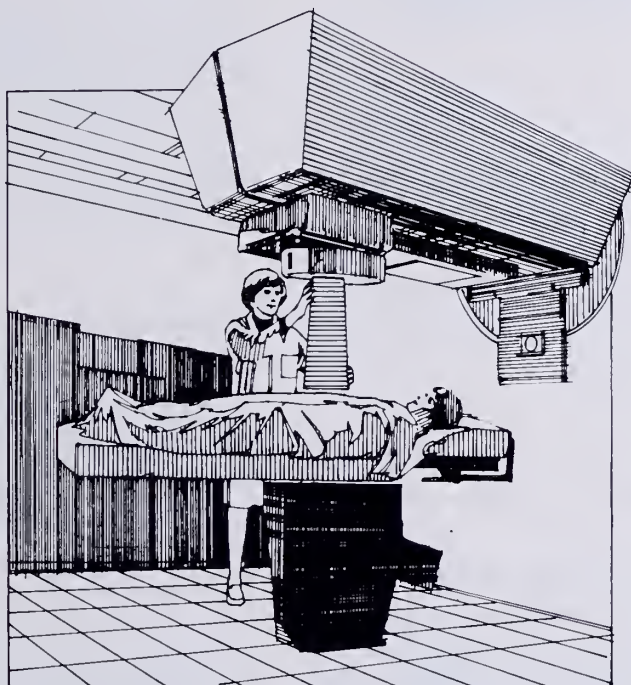


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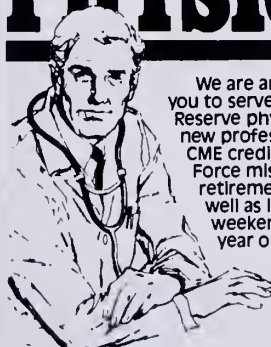
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## Index to Advertisers

Avanti .....	6
Bristol-Myers Squibb Company - Pravachol .....	third and fourth cover
CancerPay Plus .....	255
CompHealth .....	257
Disability Determination .....	256
Eli Lilly & Co. - Humulin .....	232
Employer Plus, Inc. ....	4
Medical Assurance Co. of MS .....	250
Medley and Company .....	254
MS Emergency Association .....	257
MS Physicians Insurance Company .....	252
MSMA Benefit Plan & Trust .....	second cover
Premier Printing .....	242
The Doctors' Company .....	237
Trustmark .....	242
US Air Force Reserve .....	257
US Army Active .....	231
US Army Reserve .....	249



## **PRAVACHOL® (Pravastatin Sodium Tablets)**

### **CONTRAINDICATIONS**

Hypersensitivity to any component of this medication.

Active liver disease or unexplained, persistent elevations in liver function tests (see WARNINGS).

**Pregnancy and lactation.** Atherosclerosis is a chronic process and discontinuation of lipid-lowering drugs during pregnancy should have little impact on the outcome of long-term therapy of primary hypercholesterolemia. Cholesterol and other products of cholesterol biosynthesis are essential components for fetal development (including synthesis of steroids and cell membranes). Since HMG-CoA reductase inhibitors decrease cholesterol synthesis and possibly the synthesis of other biologically active substances derived from cholesterol, they may cause fetal harm when administered to pregnant women. Therefore, HMG-CoA reductase inhibitors are contraindicated during pregnancy and in nursing mothers. **Pravastatin should be administered to women of childbearing age only when such patients are highly unlikely to conceive and have been informed of the potential hazards.** If the patient becomes pregnant while taking this class of drug, therapy should be discontinued and the patient apprised of the potential hazard to the fetus.

### **WARNINGS**

**Liver Enzymes:** HMG-CoA reductase inhibitors, like some other lipid-lowering therapies, have been associated with biochemical abnormalities of liver function. Increases of serum transaminase (ALT, AST) values to more than 3 times the upper limit of normal occurring on 2 or more (not necessarily sequential) occasions have been reported in 1.3% of patients treated with pravastatin in the U.S. over an average period of 18 months. These abnormalities were not associated with cholestasis and did not appear to be related to treatment duration. In those patients in whom these abnormalities were believed to be related to pravastatin and who were discontinued from therapy, the transaminase levels usually fell slowly to pretreatment levels. These biochemical findings are usually asymptomatic although worldwide experience indicates that anorexia, weakness, and/or abdominal pain may also be present in rare patients.

As with other lipid-lowering agents, liver function tests should be performed during therapy with pravastatin. Serum aminotransferases, including ALT (SGPT), should be monitored before treatment begins, every six weeks for the first three months, every eight weeks during the remainder of the first year, and periodically thereafter (e.g., at about six-month intervals). Special attention should be given to patients who develop increased transaminase levels. Liver function tests should be repeated to confirm an elevation and subsequently monitored at more frequent intervals. If increases in AST and ALT equal or exceed three times the upper limit of normal and persist, then therapy should be discontinued. Persistence of significant aminotransferase elevations following discontinuation of therapy may warrant consideration of liver biopsy.

Active liver disease or unexplained transaminase elevations are contraindications to the use of pravastatin (see CONTRAINDICATIONS). Caution should be exercised when pravastatin is administered to patients with a history of liver disease or heavy alcohol ingestion (see CLINICAL PHARMACOLOGY: Pharmacokinetics/Metabolism). Such patients should be closely monitored, started at the lower end of the recommended dosing range, and titrated to the desired therapeutic effect.

**Skeletal Muscle: Rhabdomyolysis with renal dysfunction secondary to myoglobinuria has been reported with pravastatin and other drugs in this class.** Uncomplicated myalgia has also been reported in pravastatin-treated patients (see ADVERSE REACTIONS). Myopathy, defined as muscle aching or muscle weakness in conjunction with increases in creatine phosphokinase (CPK) values to greater than 10 times the upper limit of normal was reported to be possibly due to pravastatin in only one patient in clinical trials (<0.1%). Myopathy should be considered in any patient with diffuse myalgias, muscle tenderness or weakness, and/or marked elevation of CPK. Patients should be advised to report promptly unexplained muscle pain, tenderness or weakness, particularly if accompanied by malaise or fever. **Pravastatin therapy should be discontinued if markedly elevated CPK levels occur or myopathy is diagnosed or suspected. Pravastatin therapy should also be temporarily withheld in any patient experiencing an acute or serious condition predisposing to the development of renal failure secondary to rhabdomyolysis, e.g., sepsis; hypotension; major surgery; trauma; severe metabolic, endocrine, or electrolyte disorders; or uncontrolled epilepsy.**

The risk of myopathy during treatment with lovastatin is increased if therapy with either cyclosporine, gemfibrozil, erythromycin, or niacin is administered concurrently. There is no experience with the use of pravastatin together with cyclosporine. Myopathy has not been observed in clinical trials involving small numbers of patients who were treated with pravastatin together with niacin. One trial of limited size involving combined therapy with pravastatin and gemfibrozil showed a trend toward more frequent CPK elevations and patient withdrawals due to musculoskeletal symptoms in the group receiving combined treatment as compared with the groups receiving placebo, gemfibrozil, or pravastatin monotherapy. Myopathy was not reported in this trial (see PRECAUTIONS: Drug Interactions). One patient developed myopathy when clofibrate was added to a previously well tolerated regimen of pravastatin; the myopathy resolved when clofibrate therapy was stopped and pravastatin treatment continued. **The use of fibrates alone may occasionally be associated with myopathy. The combined use of pravastatin and fibrates should generally be avoided.**

### **PRECAUTIONS**

**General:** Pravastatin may elevate creatine phosphokinase and transaminase levels (see ADVERSE REACTIONS). This should be considered in the differential diagnosis of chest pain in a patient on therapy with pravastatin.

**Homozygous Familial Hypercholesterolemia.** Pravastatin has not been evaluated in patients with rare homozygous familial hypercholesterolemia. In this group of patients, it has been reported that HMG-CoA reductase inhibitors are less effective because the patients lack functional LDL receptors.

**Renal Insufficiency:** A single 20 mg oral dose of pravastatin was administered to 24 patients with varying degrees of renal impairment (as determined by creatinine clearance). No effect was observed on the pharmacokinetics of pravastatin or its 3-hydroxy isomer/metabolite (SO 31,906). A small increase was seen in mean AUC values and half-life (t<sub>1/2</sub>) for the inactive enzymatic ring hydroxylation metabolite (SO 31,945). Given this small sample size, the dosage administered, and the degree of individual variability, patients with renal impairment who are receiving pravastatin should be closely monitored.

**Information for Patients:** Patients should be advised to report promptly unexplained muscle pain, tenderness or weakness, particularly if accompanied by malaise or fever.

**Drug Interactions:** Immunosuppressive Drugs, Gemfibrozil, Niacin (Nicotinic Acid), Erythromycin. See WARNINGS: Skeletal Muscle.

**Antipyrine:** Clearance by the cytochrome P450 system was unaltered by concomitant administration of pravastatin. Since pravastatin does not appear to induce hepatic drug-metabolizing enzymes, it is not expected that any significant interaction of pravastatin with other drugs (e.g., phenytoin, quinidine) metabolized by the cytochrome P450 system will occur.

**Cholestyramine/Colestipol:** Concomitant administration resulted in an approximately 40 to 50% decrease in the mean AUC of pravastatin. However, when pravastatin was administered 1 hour before or 4 hours after cholestyramine or 1 hour before colestipol and a standard meal, there was no clinically significant decrease in bioavailability or therapeutic effect. (See DOSAGE AND ADMINISTRATION: Concomitant Therapy.)

**Warfarin:** In a study involving 10 healthy male subjects given pravastatin and warfarin concomitantly for 6 days, bioavailability parameters at steady state for pravastatin (parent compound) were not altered. Pravastatin did not alter the plasma protein-binding of warfarin. Concomitant dosing did increase the AUC and C<sub>max</sub> of warfarin but did not produce any changes in its anticoagulant action (i.e., no increase was seen in mean prothrombin time after 6 days of concomitant therapy). However, bleeding and extreme prolongation of prothrombin time has been reported with another drug in this class. Patients receiving warfarin-type anticoagulants should have their prothrombin times closely monitored when pravastatin is initiated or the dosage of pravastatin is changed.

**Cimetidine:** The AUC<sub>0-12hr</sub> for pravastatin when given with cimetidine was not significantly different from the AUC for pravastatin when given alone. A significant difference was observed between the AUC's for pravastatin when given with cimetidine compared to when administered with antacid.

**Digoxin:** In a crossover trial involving 16 healthy male subjects given pravastatin and digoxin concurrently for 9 days, the bioavailability parameters of digoxin were not affected. The AUC of pravastatin tended to increase, but the overall bioavailability of pravastatin plus its metabolites SO 31,906 and SO 31,945 was not altered.

**Gemfibrozil:** In a crossover study in 20 healthy male volunteers given concomitant single doses of pravastatin and gemfibrozil, there was a significant decrease in urinary excretion and protein binding of pravastatin. In addition, there was a significant increase in AUC, C<sub>max</sub>, and T<sub>max</sub> for the pravastatin metabolite SO 31,906. Combination therapy with pravastatin and gemfibrozil is generally not recommended.

In interaction studies with aspirin, antacids [1 hour prior to PRAVACHOL (pravastatin sodium)], cimetidine, nicotinic acid, or probucol, no statistically significant differences in bioavailability were seen when PRAVACHOL was administered.

**Other Drugs:** During clinical trials, no noticeable drug interactions were reported when PRAVACHOL was added to: diuretics, antihypertensives, digitalis, converting-enzyme inhibitors, calcium channel blockers, beta-blockers, or nitroglycerin.

**Endocrine Function:** HMG-CoA reductase inhibitors interfere with cholesterol synthesis and lower circulating cholesterol levels and, as such, might theoretically blunt adrenal or gonadal steroid hormone production. Results of clinical trials with pravastatin in males and post-menopausal females were inconsistent with regard to possible effects of the drug on basal steroid hormone levels. In a study of 21 males, the mean testosterone response to human chorionic gonadotropin was significantly reduced (p<0.004) after 16 weeks of treatment with 40 mg of pravastatin. However, the percentage of patients showing a ≥50% rise in plasma testosterone after human chorionic gonadotropin stimulation did not change significantly after therapy in these patients. The effects of HMG-CoA reductase inhibitors on spermatogenesis and fertility have not been studied in adequate numbers of patients. The effects, if any, of pravastatin on the pituitary-gonadal axis in pre-menopausal females are unknown. Patients treated with pravastatin who display clinical evidence of endocrine dysfunction should be evaluated appropriately. Caution should also be exercised if an HMG-CoA reductase inhibitor or other agent used to lower cholesterol levels is administered to patients also receiving other drugs (e.g., ketoconazole, spiroclonolone, cimetidine) that may diminish the levels or activity of steroid hormones.

**CNS Toxicity:** CNS vascular lesions, characterized by perivascular hemorrhage and edema and mononuclear cell

infiltration of perivascular spaces, were seen in dogs treated with pravastatin at a dose of 25 mg/kg/day, a dose that produced a plasma drug level about 50 times higher than the mean drug level in humans taking 40 mg/day. Similar CNS vascular lesions have been observed with several other drugs in this class.

A chemically similar drug in this class produced optic nerve degeneration (Wallerian degeneration of retinogeniculate fibers) in clinically normal dogs in a dose-dependent fashion starting at 60 mg/kg/day, a dose that produced mean plasma drug levels about 30 times higher than the mean drug level in humans taking the highest recommended dose (as measured by total enzyme inhibitory activity). This same drug also produced vestibulocochlear Wallerian-like degeneration and retinal ganglion cell chromatolysis in dogs treated for 14 weeks at 180 mg/kg/day, a dose which resulted in a mean plasma drug level similar to that seen with the 60 mg/kg dose.

**Carcinogenesis, Mutagenesis, Impairment of Fertility:** In a 2-year study in rats fed pravastatin at doses of 10, 30, or 100 mg/kg body weight, there was an increased incidence of hepatocellular carcinomas in males at the highest dose (p<0.01). Although rats were given up to 125 times the human dose (HD) on a mg/kg body weight basis, their serum drug levels were only 6 to 10 times higher than those measured in humans given 40 mg pravastatin as measured by AUC.

The oral administration of 10, 30, or 100 mg/kg (producing plasma drug levels approximately 0.5 to 5.0 times human drug levels at 40 mg) of pravastatin to mice for 22 months resulted in a statistically significant increase in the incidence of malignant lymphomas in treated females when all treatment groups were pooled and compared to controls (p<0.05). The incidence was not dose-related and male mice were not affected.

A chemically similar drug in this class was administered to mice for 72 weeks at 25, 100, and 400 mg/kg body weight, which resulted in mean serum drug levels approximately 3, 15, and 33 times higher than the mean human serum drug concentration (as total inhibitory activity) after a 40 mg oral dose. Liver carcinomas were significantly increased in high-dose females and mid- and high-dose males, with a maximum incidence of 90 percent in males. The incidence of adenomas of the liver was significantly increased in mid- and high-dose females. Drug treatment also significantly increased the incidence of liver adenomas in mid- and high-dose males and females. Adenomas of the eye Harderian gland (a gland of the eye of rodents) were significantly higher in high-dose mice than in controls.

No evidence of mutagenicity was observed *in vitro*, with or without rat-liver metabolic activation, in the following studies: microbial mutagen tests, using mutant strains of *Salmonella typhimurium* or *Escherichia coli*; a forward mutation assay in L5178Y TK +/− mouse lymphoma cells; a chromosomal aberration test in hamster cells, and a gene conversion assay using *Saccharomyces cerevisiae*. In addition, there was no evidence of mutagenicity in either a dominant lethal test in mice or a micronucleus test in mice.

In a study in rats, with daily doses up to 500 mg/kg, pravastatin did not produce any adverse effects on fertility or general reproductive performance. However, in a study with another HMG-CoA reductase inhibitor, there was decreased fertility in male rats treated for 34 weeks at 25 mg/kg body weight, although this effect was not observed in a subsequent fertility study when this same dose was administered for 11 weeks (the entire cycle of spermatogenesis, including epididymal maturation). In rats treated with this same reductase inhibitor at 180 mg/kg/day, seminiferous tubule degeneration (necrosis and loss of spermatogenic epithelium) was observed. Although not seen with pravastatin, two similar drugs in this class caused drug-related testicular atrophy, decreased spermatogenesis, spermatocytic degeneration, and giant cell formation in dogs. The clinical significance of these findings is unclear.

**Pregnancy: Pregnancy Category X:** See CONTRAINDICATIONS.

Safety in pregnant women has not been established. Pravastatin was not teratogenic in rats at doses up to 1000 mg/kg daily or in rabbits at doses of up to 50 mg/kg daily. These doses resulted in 20x (rabbit) or 240x (rat) the human exposure based on surface area (mg/meter<sup>2</sup>). However, in studies with another HMG-CoA reductase inhibitor, skeletal malformations were observed in rats and mice. PRAVACHOL (pravastatin sodium) should be administered to women of child-bearing potential only when such patients are highly unlikely to conceive and have been informed of the potential hazards. If the woman becomes pregnant while taking PRAVACHOL, it should be discontinued and the patient advised again as to the potential hazards to the fetus.

**Nursing Mothers:** A small amount of pravastatin is excreted in human breast milk. Because of the potential for serious adverse reactions in nursing infants, women taking PRAVACHOL should not nurse (see CONTRAINDICATIONS).

**Pediatric Use:** Safety and effectiveness in individuals less than 18 years old have not been established. Hence, treatment in patients less than 18 years old is not recommended at this time. (See also PRECAUTIONS: General.)

### **ADVERSE REACTIONS**

Pravastatin is generally well tolerated, adverse reactions have usually been mild and transient. In 4-month long placebo-controlled trials, 1.7% of pravastatin-treated patients and 1.2% of placebo-treated patients were discontinued from treatment because of adverse experiences attributed to study drug therapy; this difference was not statistically significant. In long-term studies, the most common reasons for discontinuation were asymptomatic serum transaminase increases and mild, non-specific gastrointestinal complaints. During clinical trials the overall incidence of adverse events in the elderly was not different from the incidence observed in younger patients.

**Adverse Clinical Events:** All adverse clinical events (regardless of attribution) reported in more than 2% of pravastatin-treated patients in the placebo-controlled trials are identified in the table below; also shown are the percentages of patients in whom these medical events were believed to be related or possibly related to the drug.

Body System/Event	All Events %		Events Attributed to Study Drug %	
	Pravastatin (N = 900)	Placebo (N = 411)	Pravastatin (N = 900)	Placebo (N = 411)
Cardiovascular				
Cardiac Chest Pain	4.0	3.4	0.1	0.0
Dermatologic				
Rash	4.0*	1.1	1.3	0.9
Gastrointestinal				
Nausea/Vomiting	7.8	2.1	2.9	3.4
Diarrhea	6.2	5.6	2.0	1.9
Abdominal Pain	5.4	6.9	2.0	3.9
Constipation	4.0	7.1	2.4	5.1
Flatulence	3.3	3.6	2.7	3.4
Heartburn	3.3	1.9	2.0	0.7
General				
Fatigue	3.8	3.4	1.9	1.0
Chest Pain	3.7	1.9	0.3	0.2
Influenza	2.4*	0.7	0.0	0.0
Musculoskeletal				
Localized Pain	10.0	9.0	1.4	1.5
Myalgia	2.7	1.0	0.6	0.0
Nervous System				
Headache	6.2	3.9	1.7*	0.2
Dizziness	3.3	3.2	1.0	0.5
Renal/Genitourinary				
Urinary Abnormality	2.4	2.9	0.7	1.2
Respiratory				
Common Cold	7.0	6.3	0.0	0.0
Rhinitis	4.0	4.1	0.1	0.0
Cough	2.6	1.7	0.1	0.0

\*Statistically significantly different from placebo.

The following effects have been reported with drugs in this class:

**Skeletal:** myopathy, rhabdomyolysis.

**Neurological:** dysfunction of certain cranial nerves (including alteration of taste, impairment of extra-ocular movement, facial paresis), tremor, vertigo, memory loss, paresthesia, peripheral neuropathy, peripheral nerve palsy.

**Hypersensitivity Reactions:** An apparent hypersensitivity syndrome has been reported rarely which has included one or more of the following features: anaphylaxis, angioedema, lupus erythematosus-like syndrome, polymyalgia rheumatica, vasculitis, purpura, thrombocytopenia, leukopenia, hemolytic anemia, positive ANA, ESR increase, erythema multiforme, hepatitis, photosensitivity, fever, chills, flushing, malaise, dyspnea, toxic epidermal necrolysis, erythema multiforme, including Stevens-Johnson syndrome.

**Gastrointestinal:** pancreatitis, hepatitis, including chronic active hepatitis, cholestatic jaundice, fatty change in liver, and, rarely, cirrhosis, fulminant hepatic necrosis, and hepatoma, anorexia, vomiting.

**Reproductive:** gynecomasia, loss of libido, erections dysfunction.

**Eye:** progression of cataracts (lens opacities), ophthalmoplegia.

**Laboratory Test Abnormalities:** Increases in serum transaminase (ALT, AST) values and CPK have been observed (see WARNINGS).

Transient, asymptomatic eosinophilia has been reported. Eosinophil counts usually returned to normal despite continued therapy. Anemia, thrombocytopenia, and leukopenia have been reported with other HMG-CoA reductase inhibitors.

**Concomitant Therapy:** Pravastatin has been administered concurrently with cholestyramine, colestipol, nicotinic acid, probucol and gemfibrozil. Preliminary data suggest that the addition of either probucol or gemfibrozil to therapy with lovastatin or pravastatin is not associated with greater reduction in LDL-cholesterol than that achieved with lovastatin or pravastatin alone. No adverse reactions unique to the combination or in addition to those previously reported for each drug alone have been reported. Myopathy and rhabdomyolysis (with or without acute renal failure) have been reported when another HMG-CoA reductase inhibitor was used in combination with immunosuppressive drugs, gemfibrozil, erythromycin, or lipid-lowering doses of nicotinic acid. Concomitant therapy with HMG-CoA reductase inhibitors and these agents is generally not recommended. (See WARNINGS: Skeletal Muscle and PRECAUTIONS: Drug Interactions.)

### **OVERDOSAGE**

There have been no reports of overdoses with pravastatin.

Should an accidental overdose occur, treat symptomatically and institute supportive measures as required.



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Please see CONTRAINDICATIONS, WARNINGS, PRECAUTIONS, and ADVERSE REACTIONS in the brief summary of prescribing information on the adjacent page.



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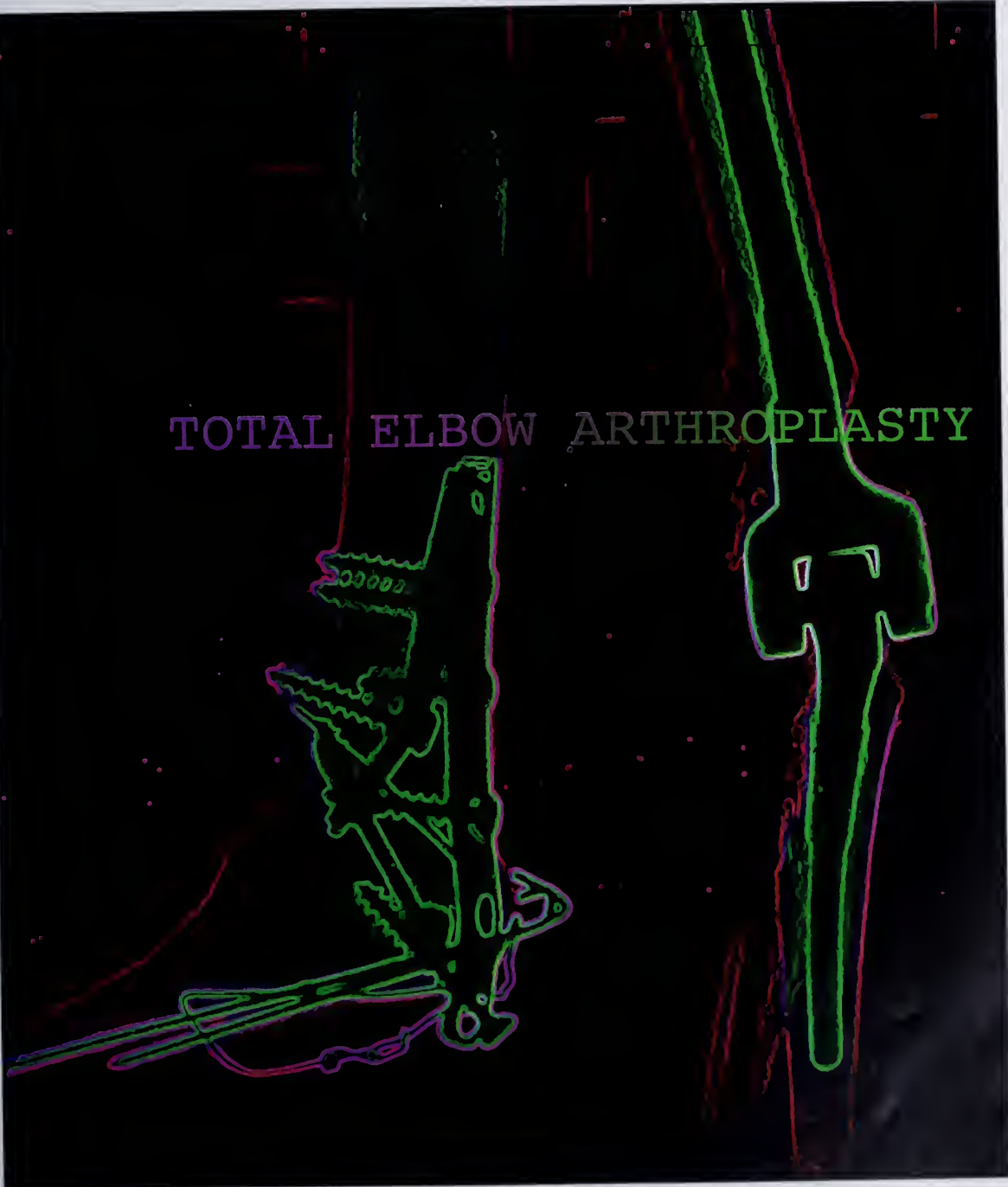
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VOLUME XXXIV

NUMBER 8

## SCIENTIFIC ARTICLES

- Total Elbow Arthroplasty: Salvage Of  
Unsuccessful Previous Elbow Surgery** 259

*Felix, H. Savoie, III, MD*

- Testicular Vein and Peripheral Vein Testosterone,  
Follicle Stimulating Hormone, Luteinizing  
Hormone, and Prolactin Concentrations In A  
Patient With Androgen Insensitivity Syndrome** 263

*G. Rodney Meeks, MD; Neil S. Whitworth, PhD and  
Melanie S. Renfroe, MD*

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## SPECIAL ARTICLE

- 1993 Annual Meeting Of The AMA House  
Of Delegates** 269

## EDITORIALS

- Why A Tree Falls** 276

*Don Q. Mitchell, MD*

- The Law Regarding Utilization Review** 277

*Myron W. Lockey, MD, Editor*

- Affordable Health Care** 278

*W. Moncure Dabney, MD, Editor Emeritus*

## DEPARTMENTS

- Medical Organization** 281

- The University of Mississippi Medical Center** 290

- Personals** 293

- Placement Service** 296

- Classified** 298

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## Gholston Elected Chairman of Board

Jackson, MS — Linda Gholston of Tupelo, formerly of Baldwin was selected as chairman of the State Board of Health.

Ms. Gholston, a vice president at North Mississippi Medical Center, is the first woman and first nurse to ever hold the office. She was the recently elected chairman of the 13 member committee by fellow committee members.

"I am excited about this new challenge, especially the prospect of working with the State Department of Health, as we begin the first phases of health care reform. All 13 of our board members are dedicated to the health and well-being of the citizens of Mississippi. We are very fortunate to work with a Department of Health that has been recognized nationally as one of the best in the country," said Ms. Gholston, who was appointed to a six-year term by Governor Ray Mabus in 1991.

Maurice James, MD, and ophthalmologist in private practice is the board's newly elected vice-chairman.

\*\*\*

## Mississippi Teen Birth- rate

Washington, DC — U. S. teen births are on the rise, and Mississippi's rate remains one of the highest, the Children's Defense Fund reports.

"Teenage childbearing too often launches both mother and child into a lifetime cycle of poverty and dependency," said Marian Wright Edelman, CDF president.

Among findings of the report:

- In 1990, the last year for which complete figures are available, Mississippi topped all but the District of Columbia in births per 1,000 girls ages 15-19.

- Mississippi's rate of 84.3 births per 1,000 girls was down from 86.6 a decade earlier.

- About 73 percent of the teen mothers in Mississippi were unmarried, compared to 67.6 percent nationally.

A state health official said the decrease in teen births was gratifying but the overall number of young mothers was discouraging.

"We have continued to really counsel patients as far as family planning is concerned, particularly when we get them in prenatal care," said Dr. Ken Pittman, a consultant in obstetrics and gynecology for the Department of Health. "That's one thing that might have had some impact on it."

Legislators approved a comprehensive education program for public school students that will cover pregnancy and its consequences, he said.

(continued)

## McDonald's Participates In Immunization Program

## MS Number One For Enforcing Water Standards

Pittman noted the 15.4 percentage point decrease in teen births in West Virginia, where a similar school initiative started. The curriculum included family planning and setting lifetime goals and priorities, he said. "It sounds like something we hope to have here in Mississippi," he said.

\*\*\*

Sardis, MS — Three-quarters of a million McDonald's diners will come face-to-face with immunization messages this summer.

Through a partnership with Mississippi Children's Immunization Project, 84 McDonald's restaurants will distribute trayliners with an important message. Each trayliner will urge parents to immunize their children before age two. Restaurants from Southaven to Pascagoula, Vicksburg to Meridian, will use the immunization trayliners three full weeks during June July and August — the heavy-traffic time for youngsters and their parents. "We are delighted and proud to have McDonald's helping in getting the word out, said Dr. Robert Abney, Awareness Project director.

"Early childhood immunizations will prevent measles, mumps, meningitis, whooping cough, lock-jaw, polio and diphtheria," the liners proclaim. "Mississippi's goal is to have ALL our children vaccinated by 2000.

"We believe this effort will reach many parents who otherwise might not remember to get their children immunized," Dr. Abney said.

The Immunization Awareness Project combines the efforts to the Mississippi Chapter of the American Academy of Pediatrics, Mississippi Nurses Association, Mississippi State Department of Health and McDonald's Restaurants.

\*\*\*

Jackson, MS — Mississippi ranks first in the nation for enforcing new standards to eliminate high lead and copper levels in drinking water. In conforming with the Environmental Protection Agency's Lead and Copper Rule, Mississippi became the first state to develop a comprehensive testing system. About 1,300 public water supply systems, or almost 80 percent of Mississippi's public water utilities, await the results of the state's first battery of tests.

"The Lead and Copper Rule went into effect in January 1992," said David Mitchell, director of the Division of Water Supply, Mississippi State Department of Health. "A lot of states have basically said they can't handle it. It's too difficult for them to set up." Under the Lead and Copper Rule, the EPA requires states to monitor lead and copper levels in all public water supplies. Any water system daily serving more than 15 connections or 25 people constitutes a public water supply. Mississippi health officials regulate more than 1,650 public water supplies. Each year, the Bureau of Environmental Health oversees the construction of about 600 new community water projects.

Mississippi is one of the few states in the country where the state government does all monitoring for the Safe Drinking Water Act.

\*\*\*



# Total Elbow Arthroplasty: Salvage Of Unsuccessful Previous Elbow Operations

FELIX H. SAVOIE, III, MD

Injuries to the elbow joint are among the most difficult to manage. Excellent surgical reconstruction of severe fractures may be defeated by underlying patient disease, stiffness or instability. In many instances the patient is instructed to attempt to live with the resulting impairment as further surgical reconstruction is usually unsuccessful. Elbow replacement, however, may allow the patient to regain a functional arc of motion as well as provide stability to the elbow joint. In this report we present our results with six multi-operated elbows reconstructed by semiconstrained total elbow arthroplasty and soft tissue reconstruction.

### MATERIALS AND METHODS

Six patients, each with a failure of two or more previous surgical reconstructions were noted to have a painful, restricted elbow that interfered with the activities of daily living. Two of the patients had rheumatoid arthritis and four patients were post-traumatic. Three right elbow

Six consecutive patients with a stiff, painful, nonfunctional elbow were reconstructed utilizing a semiconstrained total elbow prosthetic replacement. All patients had multiple previous surgical procedures with unsuccessful results. The average preoperative flexion (80 degrees) and extension (-60 degrees) improved to 130 degrees to -10 degrees respectively. All patients were able to regain satisfactory use of the elbow without pain.

and three left elbows were involved. The dominant arm was involved in five of the six patients. The prior surgical procedures included synovectomy (2 patients), radial head excision (2 patients), open reduction and internal fixation (3 patients), olecranon resection (1 patient), unconstrained total elbow arthroplasty (2 patients), irrigation and debridement (3 patients, multiple surgeries). The average number of surgeries per patient was four with a range of two to eight.

Each patient was noted to have marked functional impairment prior to consideration for surgical reconstruction. The average preoperative flexion was

80 degrees, range 60 to 110 and the average extension was -60 degrees (range -40 to -80).

All patients were asked to quantify their pain based on a simple rating scale developed by Jones and Savoie (Table I).<sup>2</sup> The average preoperative pain rating was 3.8 (range 2-4).

Table I: Pain Rating Scale

- |  |
|--|
| 0: No pain   |
| 1: Mild pain (no medicine required)                            |
| 2: Moderate pain (pain at night, occasional medicine required) |
| 3: Severe pain (regular use of medicines, impaired ADL)        |
| 4: Complete disability (patient unable to use elbow)           |

## METHODS

Each patient was reconstructed by a combination of soft tissue release/rebalancing and cemented semiconstrained total elbow arthroplasty. A standard Bryan approach to the elbow was utilized with anterior transposition of the ulnar nerve and complete evaluation of both the soft tissue and bony components of the elbow.<sup>1</sup> An intra-operative radiograph was often helpful due to the destruction of the joint to determine the correct positioning of the elbow components prior to final implantation.

The patient was splinted in full extension via an anterior splint for night protection and allowed to utilize the arm as tolerated during the day. Therapeutic exercises for the hand and wrist were initiated immediately, but no specific elbow exercises were utilized unless there was a functional deficit in the postoperative course.

## RESULTS

All six patients improved significantly over their preoperative functional level. The average flexion improved from 80 degrees to 120 degrees (range 90-135 degrees). The average extension improved to -10 degrees (range 0 to -60 degrees).

The average pain score improved from 3.8 to 0.5. All patients were able to utilize the affected arm for routine daily activities.

## COMPLICATIONS

Two patients (33%) sustained complications. One patient with a previous infection re-developed a fistula (case report #2). This resolved with a repeat debridement and antibiotic therapy with a satisfactory result.

One patient with severe rheumatoid arthritis fractured the ce-

ment bone interface of the prosthesis when he slammed his forearm on a door facing trying to stop his wheelchair from sliding through the aforementioned doorway. He was re-cemented with satisfactory result.

## CASE REPORTS • FIGURE LEGENDS

**Case #1:** This is a 40 year old left hand dominant female who was involved in a severe motor vehicle accident sustaining multiple injuries to her chest, abdomen, cervical spine, shoulder, knee, ankle and left elbow. She was appropriately managed by the polytrauma service with excellent stabilization of her multiple injuries with the exception of her elbow. The left elbow injury was a fracture dislocation (Figure 1). Initial attempt at open reduction and internal fixation was unsuccessful (Figure 2), and an excision of the olecranon and triceps reconstruction was accomplished. The extensive soft tissue injury was not appreciated and the elbow became dislocated (Figure 3). Due to the multiple injuries, repeat surgery could not be accomplished, resulting in a dysfunctional elbow with only 30 degrees to 70 degrees of motion and mild to moderate pain (Figure 4). Primary complaints centered on the inability to use the arm for daily activities including eat-

ing, dressing and personal hygiene. Due to a gradual worsening of the functional deficit, surgical reconstruction with soft tissue rebalancing was attempted. A semiconstrained prosthesis was implanted (Figure 5). Postoperatively the patient did very well with minimal to no pain, nearly full extension and flexion (Figure 6, Figure 7). She was able to perform all of her daily activities and returned to gainful employment as a teacher.



Figure 1



Figure 2



Figure 3





Figure 4



Figure 7



Figure 8



Figure 5



Figure 6

**Case #2:** This is a 78 year old female who fell sustaining a markedly comminuted fracture dislocation of the elbow. An excellent surgical reconstruction was performed by the managing

orthopaedic surgeon (Figure 8). The patient developed a wound infection, necessitating metal removal, irrigation and debridement. The elbow failed to unite and developed a complete loss of flexion and extension (Range 80 degrees to 80 degrees). There was also dysfunction of the medial collateral ligament, preventing any use of the arm as well as allowing marked instability induced ulnar neuritis (Figure 9). The patient had a semiconstrained elbow arthroplasty utilizing antibiotic impregnated ce-

ment and medial soft tissue rebalancing. During the surgery the medial epicondyle was noted to be completely avascular due to the original injury. It was essentially removed leaving a shell to allow better soft tissue reconstruction (Figure 10). One month postoperatively she discontinued

her oral antibiotics and developed recurrent drainage. She had two additional irrigation and debridement procedures and six weeks of intravenous antibiotics with eventual satisfactory out-



Figure 9



Figure 10

come. The current result is that of an elbow completely free of pain with -10 degrees of extension and 150 degrees of flexion (Figure 11, 12).



Figure 11



Figure 12

## DISCUSSION

The elbow is one of the most complex articulations of the body and its normal function is the key to being able to utilize the upper extremity. Morrey has previously delineated a functional range of motion of the elbow to be 30 to 110 degrees.<sup>3</sup> The elbow is composed of three separate joints, ulnohumeral, radiocapitellar and proximal radioulnar. All must move smoothly to provide this functional use of the elbow. Static stability is afforded by the medial and lateral (radio-

ulnohumeral) ligaments, and dynamic stability by the flexor-pronator (medial) and extensor (lateral) muscle groups.

Destructive arthritic disease may produce damage to this area that is not reconstructible by conventional means. Morrey has presented both short and long term follow-up studies of semiconstrained elbow arthroplasty with excellent results in these patients.<sup>4</sup> Although nonconstrained prostheses are available, the extensive destruction in these patients precludes the use of these implants.<sup>5</sup> In studies from the Mayo Clinic the semiconstrained prosthesis was noted to provide results equal to the unconstrained in loosening and to provide a lower incidence of associated complications, including ulnar neuropathy and instability.<sup>4</sup>

The utilization of elbow arthroplasty to reconstruct failed surgical procedures has only recently been appreciated.<sup>5</sup> In this group of severely injured individuals conventional surgical procedures did not provide satisfactory results despite excellent initial procedures. These patients were referred to our clinic as a last resort. Although all patients are not candidates for this extensive procedure, the results obtained in these patients seem to justify the use of this technique. Comparison to reported series of primary total elbow replacement reveals the patients in this series obtained similar relief of pain and improved functional ability.<sup>1,3-5</sup>

In conclusion, semiconstrained prosthetic replacement provided satisfactory results in this series of severe elbow inju-

ries. □

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# Testicular Vein and Peripheral Vein Testosterone, Follicle Stimulating Hormone, Luteinizing Hormone, and Prolactin Concentrations In A Patient With Androgen Insensitivity Syndrome

G. RODNEY MEEKS, MD  
NEIL S. WHITWORTH, PhD  
MELANIE S. RENFROE, MD

Complete androgen insensitivity syndrome (testicular feminization) was first described by Morris in 1953.<sup>1</sup> It is the most common form of familial male pseudohermaphroditism and has an incidence of 1/60,000 phenotypic females.<sup>2</sup> Phenotypic females with an XY karyotype are often seen by the physician because of inguinal hernia before puberty or primary amenorrhea after puberty.<sup>3</sup> The patient usually has well-defined female psychosexual orientation and libido. The habitus is feminine and the breasts are well-developed. However, the nipples are juvenile with pale areolae. Axillary, facial, pubic, and vulvar hair are scanty or absent. Scalp hair is female. The external genitalia are feminine in appearance but infantile in the degree of development (particularly labia minora). The vagina may be absent, rudimentary, or short and blind-ending. The cervix and uterus are absent, although rudimentary analage resembling fallopian tubes

Androgen insensitivity syndrome (testicular feminization) is classically diagnosed by history, physical examination, karyotype and ultimately exploratory laparotomy. In this case, the diagnosis was verified by amenorrhea, female phenotype, Barr body negative buccal smear, and finally, exploratory laparotomy which revealed bilateral abdominal testes. Testicular vein blood samples obtained at the time of surgery were analyzed for testosterone, follicle stimulating hormone, luteinizing hormone, and prolactin and compared to peripheral vein blood samples. The testosterone concentration in the testicular vein was twice the concentration in the peripheral sample, reflecting gonadal function. The other testicular vein hormone concentrations mirrored the peripheral vein concentrations.

or spermatic cords may be present. The gonads histologically resemble undescended testes and are ordinarily found in the abdominal cavity, along the inguinal canal, or in the labia majora.<sup>4</sup> The seminiferous tubules are small and lined predominantly with Sertoli cells. Leydig cell hyperplasia is present and very little if any spermatogenesis is seen.<sup>4</sup>

The fetal testes produce Mul-

lerian inhibiting factor, therefore, female internal genitalia do not develop. The only internal genitalia are undescended testes. The testes also produce testosterone but no virilization or masculinization occurs because the target organs do not bind testosterone. The external genitalia are female because of a lack of response to testosterone.<sup>5</sup> The lack of testosterone binding is due to the absence or an abnormal structure

of the cytosol androgen receptor molecule.<sup>6</sup> Nuclear extracts of cells from patients with complete androgen insensitivity syndrome show normal binding of testosterone.<sup>7</sup>

The absence of androgen binding in the anterior pituitary results in a defect in feedback regulation of luteinizing hormone (LH). The elevated LH concentration stimulates gonadal steroidogenesis resulting in a serum testosterone concentration which is normal or slightly above normal for men.<sup>1</sup> Dihydrotestosterone concentration is also normal because 5- $\alpha$  reductase is normal. The lack of masculinizing androgen response coupled with peripheral androgen conversion to estrogen produces a phenotypic female during fetal life and the development of secondary female sexual characteristics at the time of puberty. Estrogen concentration, however, is not in the normal female range and does not inhibit LH production.<sup>3</sup>

Because the risk of malignancy approaches 33% in the undescended testis, the gonads should be removed.<sup>8</sup> However, castration should be delayed until after puberty to allow secondary sexual characteristics to develop since the risk of malignancy does not increase significantly until after 30 years of age. Once the patient is castrated, estrogen replacement therapy should be instituted.

Complete androgen insensitivity syndrome may be either an X-linked recessive or a male-limited autosomal dominant trait with the cytosol androgen receptor locus being on the X chromosome.<sup>9</sup> Incomplete androgen insensitivity syndrome is also an inherited disorder but is distinctly different from the complete syndrome. The two disorders

are not found within the same family.<sup>4,6</sup> Both syndromes are characterized by female phenotype, but the incomplete form has some degree of virilization. Wolffian duct derivatives may be present and the external genitalia may be ambiguous with labial fusion and clitoromegaly.<sup>10</sup> Gender assignment is best made as female.

## CASE REPORT

AM, an 18-year-old black, phenotypic female had a well developed rugated vagina but no uterus or cervix. Breast development was Tanner stage IV, axillary hair was absent, pubic hair was minimal, and the clitoris and labia minora were infantile.

Buccal smear showed 0/100 cells containing Barr bodies (normal female  $30 \pm 5\%$ ; normal male  $< 3\%$ ) and 56/100 cells containing Y-bodies (normal female  $< 12\%$ ; normal male  $> 50\%$ ). Giemsa banding karyotype revealed 46, XY, 9qh\*(a normal variant). Peripheral vein blood samples were obtained prior to, during, and 48 hours after surgery. Testicular vein blood samples were obtained during exploratory laparotomy.

The preoperative peripheral vein testosterone concentration was 1190 ng/dl and the peripheral LH concentration was 31 mIU/ml, both of which are above the normal male concentration. Both follicle stimulating hormone (FSH) and prolactin (PRL) were within the normal limits. The intra-operative peripheral vein samples for testosterone, LH, and FSH were not significantly different from the pre operative values. However, the PRL concentration was approximately six times the preoperative concentration. The testicular vein samples were obtained before gonadectomy. The testosterone

concentration was 2400 ng/dl on the right side and 2160 ng/dl on the left. The other hormone concentrations were similar to the intraoperative peripheral vein sample. Postoperatively, the testosterone concentration decreased to 14 ng/dl and LH decreased to 13 mIU/ml. Prolactin remained slightly elevated and FSH remained normal. These values are summarized in Table I.

Bilateral gonadectomy was performed. Each gonad was firm and the tunica albuginea was smooth, gray and glistening. Each was approximately 3 cm x 2 cm x 2 cm and had an unremarkable epididymis attached. The cut surface was somewhat soft and showed two distinct areas - a capsular area which was gray and a central area which was yellow. Histological examination revealed immature seminiferous tubules lined by Sertoli cells and well-defined Leydig cell hyperplasia. No spermatogenesis was present (Figure 1). Estradiol valerate in oil 40 mg was given immediately after surgery, and the patient was started on conjugated estrogen 1.25 mg daily on the first postoperative day.

## DISCUSSION

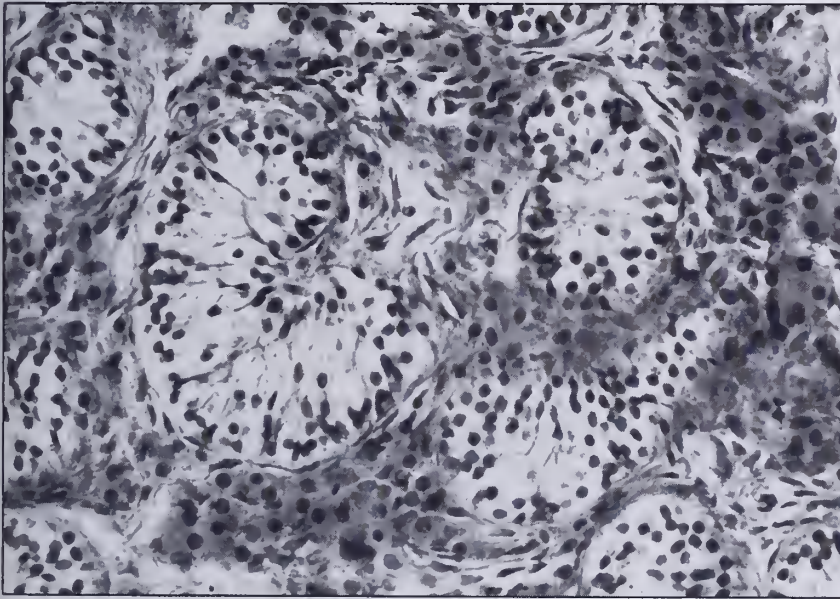
The preoperative peripheral vein samples are similar to those described by others and indeed would make one suspect androgen insensitivity syndrome.<sup>2,3</sup> The LH concentration is elevated to approximately three times normal because of the defect in feedback regulation to the anterior pituitary. In turn, the testosterone concentration is slightly above the normal limit because of excessive LH stimulation of the gonadal stroma. Prolactin and FSH are normal.

The intraoperative peripheral vein concentration of PRL is in-



**Table I HORMONE CONCENTRATIONS**

Hormone	Peripheral Vein			Testicular Vein		Normal Value	
	(Pre-op)	(Intra-op)	(Post-op)	Right	Left	Male	Female
Testosterone (ng/dl)	1190	1140	14	2400	2160	300-100	20-86
LH (mIU/ml)	31	39	13	39	37	0-9	3-25
FSH (mIU/ml)	5	3	5	7	6	2-10	5-18
PRL (ng/dl)	4	20	16	16	28	0-11	0-19



*Figure 1. Microscopic section (400x) of the gonad. Immature seminiferous tubules are lined by Sertoli cells and well-defined Leydig cell hyperplasia is present. Spermatogenesis is absent.*

creased approximately six-fold, and most likely is the result of the stress of surgery. The other values are unchanged. Testicular vein samples showed a testosterone concentration twice that of the peripheral vein concentration indicating the gonad's function as a source of testosterone. The other hormone concentrations were similar to the intraoperative peripheral vein concentrations

and indicate that the gonad does not modify LH, FSH, or PRL concentration.

The postoperative peripheral vein testosterone concentration decreased markedly and reflects removal of the source of testosterone. The decline in testosterone concentration occurred in just 48 hours and reflects rapid degradation of testosterone. The decline of the LH concentration

is likely secondary to the estrogen suppressing effect on the anterior pituitary. The PRL concentration remains slightly above normal. This may be a residual effect from the stress of surgery or possibly mild stimulation from the estrogen replacement.

Exploratory surgery to verify that the gonads are testes has historically provided definitive means of diagnosing androgen insensitivity syndrome. Serum androgen studies are also of value since testosterone concentration is within or above the normal male range. Testicular vein samples, however, may provide more clear-cut evidence of this syndrome, particularly if confusion exists concerning the diagnosis or function of the gonads. The testosterone concentration is higher in the testicular vein sample than in the peripheral vein. Testicular vein samples were obtained directly at surgery in the case presented. These samples could, however, be obtained by selective venous catheterization.

Testicular vein or ovarian vein samples may also be useful in other situations. For example, in cases where unilateral hor-

mone-producing tumors are present, the venous sample on the side of the tumor would clearly show an elevated steroid level. Also in conditions which affect both gonads equally such as polycystic ovarian disease and androgen insensitivity syndrome, the hormone concentrations would be similar in each venous sample.

This case demonstrates a classic presentation of complete androgen insensitivity syndrome. The hormone concentrations before, during, and after surgery have been shown and discussed. A technique for evaluation of gonadal function, i.e., gonad vein sampling, is discussed. This technique may have utility in other situations. □

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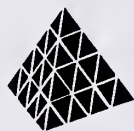
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**References** must be double spaced on a separate sheet of paper and limited to a reasonable number. They will be critically examined at the time of review and must be kept to a minimum. All references must be cited in the text and the list should be arranged in order of citation, not alphabetically. Personal Communications and unpublished data should not be included in references, but should be incorporated in the text. The following form should be followed:

#### **Journals**

[1] **Author(s).** Use the surname followed by initial without punctuation. The names of all authors should be given unless there are more than three, in which case the names of the first three authors are used, followed by "et al." [2] **Title of article.** Capitalize only the first letter of the first word. [3] **Name of Journal** followed by no punctuation, underscored or in italics, and abbreviated according to List of Journals Indexed in Index Medicus. [4] **Year of publication;** [5] **Volume number:** Do not include issue number or month except in the case of a supplement or when pagination is not consecutive throughout the volume. [6] **Inclusive page numbers.** Do not omit digits.

**Example:** Bora LI, Dannem FJ, Stanford W, et al.  
A guideline for blood use during surgery.  
*Am J Clin Pathol* 1979;71:680-692.

#### **Books**

[1] **Author(s).** Use the surname followed by initials without punctuation. The names of all authors should be given unless there are more than three, in which case the names of the first three authors are used followed by "et al." [2] **Title,** Capitalize the first and last word and each word that is not an article, preposition, or conjunction, of less than four letters. [3] **Edition number,** [4] **Editor's name.** [5] **Place of publication,** [6] **Publisher,** [7] **Year,** [8] **Inclusive page numbers.** Do not omit digits.

**Example:** DeGole EL, Spann E, Hurst RA Jr, et al.  
Bedside Examination, in Cardiovascular  
Medicine, ed 2, Smith JT (ed). New York,  
McGraw Hill Co, 1986, pp 23-27.

**Illustrations** should be submitted in duplicate in an envelope (paper clips should not be used on illustrations since the indentation they make may show on reproduction). Legends should be typed, double-spaced on a separate sheet of paper. Photographic material should be high-contrast glossy prints. Patients must be unrecognizable in photographs unless specific written consent has been obtained, in which case a copy of the authorization should accompany the manuscript. All illustrations should be referred to in the body of the text. Omit illustrations which do not increase understanding of text. **Illustrations must be limited to a reasonable number** (four illustrations should be adequate for a manuscript of 4 to 5 typed pages.) The following information should be typed on a label and affixed to the back of each illustration: figure number, title of manuscript, name of senior author, and arrow indicating top.

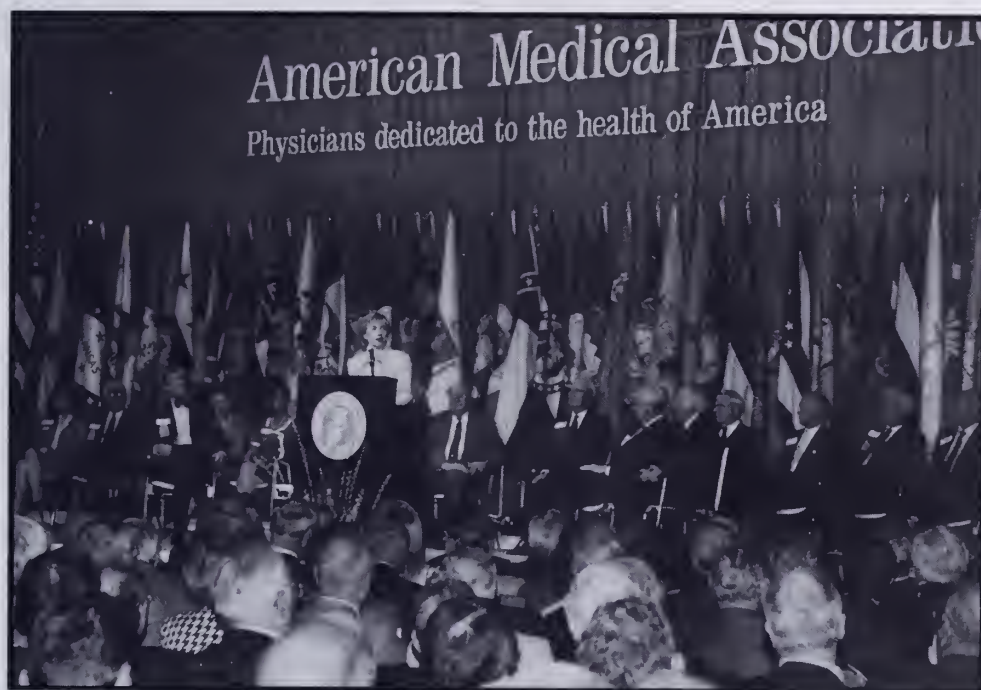
**Tables** should be self-explanatory and should supplement, not duplicate, the text. Each should be typed on a separate sheet of paper, be numbered, and have a brief descriptive title.

**Acknowledgments** are the author's prerogative; however, acknowledgment of technicians and other remunerated personnel for carrying out routine operations or of resident physicians who merely care for patients as part of their hospital duties is discouraged. More acceptable acknowledgements include those of intellectual or professional participation. The recognition of assistance should be stated as simply as possible, without effusiveness or superlatives.

**Galley Proofs** will be mailed to the principal author for corrections. Reprint order forms will accompany galley proofs. □



# 1993 Annual Meeting Of The AMA House Of Delegates



- The AMA House of Delegates met in Chicago June 13-17, 1993.
- There were 435 delegates seated, representing state medical associations, national medical specialty societies, AMA Sections, the Armed Forces, and the U.S. Public Health Service.
- The House agenda contained 117 reports and 229 resolutions.
- The First Lady, Hillary Rodham Clinton, addressed an overflow audience at the Opening Session. She spoke to many of the major concerns of physicians e.g. CLIA regulations, third party interference, professional liability reform, and quality of care.
- In his Inaugural Address AMA's new President, Joseph T. Painter, MD, (Texas) called for physicians to focus on three core values that he called the "taproots" of the medical profession. The first constant of medicine is scientific excellence; the second is the personal touch, treating each patient with respect and compassion; and the third is the application of problem-solving skills. He asked physicians to nurture their roots, carry organized medicine's message to other physicians in their communities, and apply their problem solving skills to the search for real solutions in health system reform.

A wide variety of issues were considered in socio-economics, science, medical education and public health. Following are highlights of the ma-

for issues considered at the meeting:

### **HARNESSING MARKET FORCES IN MEDICAL PRICING**

The House considered a major report of the Board and four resolutions pertaining to physician payment under Medicare RBRVS. The House took the following actions to guide the Association in the coming months:

1. That the AMA continue its policy of non-endorsement of the Medicare RBRVS-based physician payment system until such time as it is adequately corrected and refined.
2. That the AMA call for HCFA to conduct a study and collect cost data necessary for development of a resource-based approach to practice expenses for the Medicare RBRVS with all deliberate speed. In addition, that the AMA advocate that HCFA be given the authority to immediately correct identified anomalies in the current RBRVS practice expense relative value units. All applications of these methods should refrain from reductions in payments for services without complementary increases in services that this method identifies as "undervalued."
3. That the AMA advocate the following principles for physician payment under Health Access America and any other relevant health system reform proposal:
  - A. A resource-based relative value scale (RBRVS) that is annually updated and rigorously validated could be a basis for non-Medicare physician fee and payment schedules.
  - B. Payors could make their fee-for service payments with a payment schedule based on the national standard RBRVS.
  - C. Physicians could likewise base their fees on the national standard RBRVS. Fees would be based upon a physician conversion factor determined by physicians' assessment of their overhead and the market value of their services.
  - D. All third party payors using this method would provide their enrolled beneficiaries with: a copy of the current national stan-

dard RBRVS; the plan's current conversion factor; and any plan RBRVS adjusters.

- E. In managed care plans, government plans and health plans as feasible, payor conversion factors should be negotiated between individual health plans and the affected physicians.
4. That the AMA Board of Trustees provide assistance and guidance to state medical associations, national medical specialty societies, physician practices, and public and private third party payors to help ensure that any potential non-Medicare use of an RBRVS reflects the most current and accurate data and implementation methods.
5. That the AMA actively support the position that the RBRVS should not be implemented by private payors as a cost containment device. Savings from payment reductions should be used for the purpose of increasing payments for undervalued services.
6. That the AMA reaffirm policies which hold that a relative value scale, a tool for use by physicians and/or payors, is not, in and of itself, a fee schedule, and that the AMA continue its strong opposition to implementation of any mandatory fee schedule.
7. That the AMA reaffirm the policy which, as part of Health Access America, calls for employers to make available to their employees a triple option in health plans: a benefit payment schedule, a UCR plan, and a pre-paid plan.

### **HEALTH SYSTEM REFORM**

The House considered three reports and three resolutions on health system reform under consideration by the Clinton Administration. The House voted to:

- A. Reaffirm policy supporting the continuation of AMA activities to reform sensibly the Medicare program in a manner that will:
  1. examine the long-term care needs of the Medicare eligible population.
  2. address the health care needs of the next generation of Medicare beneficiaries.
  3. reduce hassles imposed on physicians, hospitals, other providers of health care ser-



vice and beneficiaries.

4. recognize the economic status of program beneficiaries.
5. address pressing funding needs.
6. address the issue of the crisis developing over rising health care costs.

B. Call for a Council on Medical Service report to the House on the following issues: (1) the extent to which a system of individually-selected and owned health insurance should be the long range goal of the AMA, (2) the feasibility of mandatory employer responsibility for ensuring that employees choose and own their own health insurance, and (3) discussions with large and small employers to determine their views and obtain their suggestions on this issue.

C. Reaffirm opposition to global budgeting, expenditure targets, price controls, and similar methods of limiting health care expenditures, yet acknowledge that some state medical associations are in favor of a budgeting process that incorporates the ability for physician groups to bargain collectively on state-level budgets and supports these state medical associations in their negotiations and development of budgeting process.

#### **REQUIRED BENEFITS PACKAGES**

The House considered a major report from the Council on Medical Service that described the process of the development of such a package, recommended criteria that should govern the general structure and the services to be covered under recommended benefit plans, and identified a recommended benefits package that the Council believes to be consistent with these criteria. Five resolutions also addressed various aspects of this issue.

The House approved the recommended benefits package proposed by the council and asked the AMA to advocate the proposal within the context of AMA's Health Access America. The House approved the recommendation that the AMA continue to encourage and support outcome studies, development of additional practice parameters based on these studies, and further refinement of the required benefits package based on such studies.

#### **REPEAL OF CLIA**

The inordinate regulatory burden imposed by CLIA engendered much debate. The Board of Trustees submitted a progress report on efforts to alleviate the CLIA regulatory burden and also reported

that more substantial relief is imminent.

The House adopted a substitute resolution from the Texas Delegation calling for AMA to:

- establish as primary policy the repeal of CLIA 88, and that the Board of Trustees provide a progress report to the House at the 1993 Interim Meeting, and
- AMA continue to work to achieve changes that markedly reduce or eliminate the obstacles experienced by physicians and Public Health Departments under CLIA.

In a related action the House voted: "that the AMA continue to support eliminating the full weight of regulatory requirements through the development of an expanded and modified free standing physician testing category that would allow physician-supervised personnel to perform tests necessary for the treatment of the physician's patients."

#### **INCREASING THE AVAILABILITY OF PRIMARY CARE**

The Council on Medical Education issued a major report that discussed the multiple factors that influence the choice of a medical career and observed that no single intervention is likely to be as effective as a multifaceted approach. The House approved 13 recommendations that addressed the medical school experience, the residency curriculum, the practice environment, and positive incentives to encourage selection of primary care specialties.

#### **NATIONAL PRACTITIONER DATA BANK**

There was extensive discussion supporting dissolution of the National Practitioner Data Bank. While commending the Board for its aggressive efforts to correct the problems with the Data Bank and recognizing that repeal may be an uphill battle, the House voted to "affirm its support for the Federation of State Medical Boards Action Data Bank and call for the dissolution of the National Practitioner Data Bank."

#### **AMA DUES**

Noting that the dues levels have remained unchanged for the past five years and that a small increase in dues is necessary to continue the AMA's advocacy activities on behalf of physicians, the House approved a recommendation to increase the dues by \$20 for 1994.

In fiscal year 1992, operating revenues for our AMA totalled \$197,474,000 and operating expenses amounted to \$193,523,000. The House commended the Board and the staff for their exemplary efforts in leading and managing the financial affairs of the AMA for the past five years without an increase in dues levels.

MSMA members may contact the MSMA office or any of Mississippi's AMA Delegates or Alternate Delegates regarding any reports or resolutions considered at the meeting. Mississippi's Delegates and Alternates are:

#### **DELEGATES:**

Sidney O. Graves, MD, Natchez  
J. Edward Hill, MD, Hollandale  
James C. Waites, MD, Laurel  
J. Elmer Nix, MD, Jackson  
William C. Gates, MD, Columbus  
Don Q. Mitchell, MD, Jackson

#### **ALTERNATE DELEGATES:**

George E. McGee, MD, Hattiesburg  
W. Joseph Burnett, MD, Oxford  
Alton B. Cobb, MD, Jackson  
Fred L. McMillan, MD, Jackson  
Candace E. Keller, MD, Hattiesburg  
W. Lamar Weems, MD, Jackson

□



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# Membership Benefits

Representation, advocacy, public relations and support of professional ethics are some of the reasons MSMA exists for its members. These are the intangible but important benefits of membership which MSMA seeks to provide through member participation. There are also more tangible benefits which the association provides its members. Illustrated here are the MSMA-sponsored programs for such member needs as insurance and practice management support. These programs are listed below.

## MEMBERSHIP HOTLINE

The MSMA provides a toll free WATS for any member to call to inquire about programs and policies of the association. Inquiries about AMA programs and policies can also be made over a membership WATS line.

## LIAISON SERVICES

MSMA conducts liaison with Travelers Medicare, Medicaid and other third party payor programs on behalf of its members. Individual claim problems, as well as general policy matters, are important aspects of this liaison. For further information call Jackye Wiebelt at MSMA.

## HEALTH INSURANCE

MSMA members who are organized as PAs and wish to provide health insurance coverage for their employees are eligible to participate in a self-insured 501(c)(9) trust sponsored and administered by a subsidiary of the association. For information contact Jackye Wiebelt at MSMA.

## BUSINESS AND PERSONAL INSURANCE

The MS Physicians Insurance Company (MPIC) in cooperation with MSMA offers a wide range of insurance for members of the association. MPIC has a Board of Directors appointed by MSMA composed entirely of practicing physicians who seek to identify the special insurance needs of physicians. For further information contact Jennifer Jones at MPIC.

## PRACTICE MANAGEMENT

Through an arrangement with the AMA Department of Practice Management, MSMA periodically conducts practice management workshops for physician's office personnel. These workshops cover a broad range of topics from CPT-IV coding to patient surveys. For further information call Jackye Wiebelt at MSMA Diversified Services, Inc.

## DEBT COLLECTION SERVICE

Based upon sponsorship by medical associations in many states and its nationwide network, IC System is endorsed by MSMA to perform debt collection services for offices and clinics of member physicians. IC System has a proven track record as a debt collection service. For further information call Robert Kidd at MSMA.

## FINANCIAL/RETIREMENT PLANNING

MSMA members by virtue of their membership in the AMA are eligible to participate in AMA Investment Advisors, Inc. This wholly owned investment subsidiary of the AMA offers a wide range of investment opportunities tailored specifically for physicians. For further information call AMA Advisers.

## MEDICAL MALPRACTICE INSURANCE

The Medical Assurance Company of MS (MACM) was sponsored and organized by MSMA in 1976 to provide a stable market for medical liability insurance to eligible physicians. More than 1500 Mississippi physicians are currently insured by MACM and extensive physician leadership is involved in all phases of MACM's operations. For further information call MACM.

**MSMA and MSMA Diversified Services** - 735 Riverside Drive, Jackson, MS 39202-1166; 601-534-5433 or 800-898-0251 (In-State-WATS).

**AMA Advisers** - 200 N. LaSalle Street, #535, Chicago, IL 60601, 800-525-0864.

**AMA and AMA Membership Hotline** - 515 North State Street, Chicago, IL 60610; 800-AMA-3211.

**Mississippi Physicians Insurance Company** - P.O. Box 5229, Jackson, MS 39296-5229, 601-354-5433 or 800-898-0251 (In-State-WATS).

**Medical Assurance Company of Mississippi** - P.O. Box 4915, Jackson, MS 39296-4915, 601-353-2000 or 800-325-4172 (In -State-WATS).



MISSISSIPPI STATE MEDICAL ASSOCIATION

# Membership Services

**When you need information on a specific subject or association service,  
the following MSMA staff person(s) are available to assist you.**

**Address Changes • Barbara Shelton**

**Advertising • Ginger Cocke**

**Annual Meetings:**

**Delegates • Barbara Shelton**

**Scientific Exhibits • Ginger Cocke**

**Technical Exhibits • Kay Gatewood**

**Meeting Schedule • Ginger Cocke**

**Bills and Invoices • Robert Kidd**

**Board of Trustees & Officers • Charles Mathews**

**CommuniCare/Complaints from the Public/  
Office /Brochures • Lora Lane**

**Continuing Medical Educations (CME) •  
Lora Lane**

**Component Medical Societies • Barbara Shelton**

**CPT/ICD-9 Inquiries • Debra Collins**

**Directories (MSMA and Auxiliary member  
listings) • Barbara Shelton**

**Dues (MSMA & Auxiliary) • Barbara Shelton**

**Government:**

**State • Clare Hester**

**National • Bill Roberts**

**Health Care Statistics and Data • Bill Roberts**

**Insurance Form Orders • Angela Martin**

***Journal MSMA* • Ginger Cocke**

**Legislative Activities • Clare Hester**

**Licensure • Bill Roberts**

**Mail Lists & Labels • Lucy Spence**

**Media (Radio, TV, Press) • Ginger Cocke**

**Medical Ethics • Bill Roberts**

**Medical Student Membership • Barbara Shelton**

**Medicare/Medicaid • Jackye Wiebelt**

**Member Benefits • Bill Roberts**

**MMPAC/AMPAC • Clare Hester**

**Physician Referrals • Lora Lane**

**Practice Management Workshops • Debra Collins**

**Public Information • Ginger Cocke**

**Resident Physician Membership • Barbara Shelton**

**Scientific Assembly • Ginger Cocke**

**Young Physician Section • Bill Roberts**

## MSMA Office

**735 Riverside Drive**

**Jackson, MS 39202**

**(601) 354-5433**

**P. O. Box 5229**

**Jackson, MS 39296-5229**

**MS WATS (800) 898-0251**

**FAX: (601) 352-4834**



## The President's Page

DON Q. MITCHELL, MD

### Why A Tree Falls

**I**t takes two things to blow down a tree — a heavy wind outside and rot and decay within. So it is with people, the winds of adversity may cause us to bend, but if we are strong and vigorous within, we will arise and grow to new heights after the storm passes." This anecdote was taken from my senior minister's March 28, 1993 column entitled "Think on These Things".

I feel that this anecdote is very appropriate to us the physicians of the MSMA in this time of massive change to our health care system. It definitely gives us some things to think about.

**Unity** among physicians is absolutely necessary for us to compete on an equal basis with the rule-makers and purchasers in any new health system. As physicians who direct the care given, we occupy a unique and central position in the system. However, our position can only be maintained if we organize and work together as one large cohesive group. If not, we will become the ones directed.

We physicians have to recognize that we do have enormous power. We should meet hospitals and third party payors as equals and not supplicants. However, I reiterate that this can only be accomplished if we are unified and in groups with sufficient size and management savvy that positions us to effectively negotiate.

Recently you received a letter from me regarding a "physician care network" that has been endorsed by your leadership. This network is being organized and will be controlled by **Mississippi physicians**. The members of this network will agree to medical review by their colleagues who are part of the network and deliver quality, cost effective care under standards set by those same colleagues. Membership in the network will be available only to members of our MSMA. If you are interested in participating in our "physicians care network" I encourage you to return the form which accompanied my letter.

The winds of adversity are clearly blowing, but if we **remain united**, we will surely succeed.

Your colleague,

A handwritten signature in dark ink, appearing to read "Don" or "DQ Mitchell".



## The Law Regarding Utilization Review

In recent months I have heard numerous complaints by physicians regarding utilization review and pre-certification decisions made by nurses and other paramedical personnel. Many have questioned the medical validity of these decisions and are enraged that a paramedical person is dictating the proposed care or care already administered to a patient and have ask "What can I do about such decisions?"

To avoid such conflicts Physicians should obtain and study copies of the "Utilization Review Law of the State of Mississippi. (Senate Bill 2393 of 1990), and the REGULATIONS FOR CERTIFICATION OF UTILIZATION REVIEW AGENTS IN MISSISSIPPI adopted and promulgated by the Mississippi State Board of Health. Understanding the law and insisting on your rights will relieve you of having to discuss any case with a nurse or other paramedical personnel. The following quotations from Senate Bill 2393, 1990, specifically states what a review agent must adhere to when conducting utilization review in the state of Mississippi.

Article 41-83-3 Paragraph (1): "A private review agent who approves or denies payment or who recommends approval or denial of payment for hospital or medical services or whose review results in approval of denial of payment for hospital or medical services on a case by case basis, may not conduct utilization review in this state unless the Mississippi State Board of Health has granted the private review agency a certificate".

Article 41-83-31 Paragraph (a): "No determination adverse to a patient or to any affected health care provider shall be made on any question relating to the necessity or justification for any form of hospital, medical or other health care services without prior evaluation and concurrence in the adverse determination by a physician. The reasons for any adverse determination shall be discussed by said physician with the affected health care provider, if the provider

so request"

Paragraph (b): "Any determination regarding hospital, medical or other health care services rendered or to be rendered to a patient which may result in a denial of third party reimbursement or denial of pre-certification for that service shall include the evaluation, findings and concurrence of a physician trained in the relevant specialty or subspecialty, if requested by the physician, to make a final determination that are rendered or to be rendered was, is, or may be medically inappropriate".

Article 41-83-21: "Notwithstanding language to the contrary elsewhere contained herein, if licensed physician certifies in writing to an insurer within seventy-two (72) hours of an admission that the insured person admitted was in need of immediate hospital care, such shall constitute a prima facie case of the medical necessity of the admission. To overcome this, the entity requesting the utilization review and/or the private review agent must show by clear and convincing evidence that the admitted person was not in need of immediate hospital care".

Part V (3) (f) of the REGULATIONS FOR CERTIFICATION OF UTILIZATION REVIEW AGENTS IN MISSISSIPPI states the following : That a private review agency shall submit the following documentation, "The policies and procedures to ensure that a representative of the private review agent is accessible to patients and providers five (5) days a week during normal business hours in this state, 9 a.m. to 5 p.m.; and that a free telephone number be provided with adequate lines available and staffed. The procedure for handling after-hours calls shall be specified".

A list of all certified agents and their certification number is available from the State Board of Health. It is to be noted that Private agents operating solely under contract with the federal government for utilization review of patients eligible for hospital services under Title XVIII of the Social Security Act (medi-

*(Continued on page 278)*

The editorial opinions expressed in this Journal are those of the indicated author. Editorial opinions are not expressions of the views, or official policies of The Mississippi State Medical Association. We encourage the membership to submit letters for publication regarding any opinion expressed or information contained in the Journal.

care] and Title XIX [medicaid] are exempted by the regulations.

The first thing a physician or their office personnel should do upon receiving a call from a utilization review agency is to request the certification number of the reviewing agency, and place that number in the patients medical record. For continued patient-physician confidentiality no patient related information should be release to anyone until a certification number has been obtained.

Second, physicians need to realize that a nurse or other paramedical person cannot independently make any decision leading to denial of services. Any physician being challenged should immediately ask for the name of the physician that the adverse decision had been discussed with, and who concurred in the adverse decision. If such discussion and concurrence has not been obtained any decision rendered by the nurse is invalid.

The third thing a physician need to do is demand that the physician for the reviewing agency discuss the case with you, but as stated in the law the physician being challenged by the reviewing agency has to request such a call. Not only do you have the legal right for such a discussion but you can demand that the reviewing physician be trained in your specialty or subspecialty. If a request is made for the reviewing physician to discuss the case with you the nurse cannot render a decision until such discussion is carried out.

The fourth thing a practicing physician needs to understand is the need for certification of the need for immediate hospital care in writing to the insurer within 72 hours of admission.

A thorough review and understanding of the Utilization Review laws of the State of Mississippi is encouraged and in doing so you will have less problem with reviewers. □

**Myron Lockey, MD**  
**Editor**

## **Affordable Health Care**

We may as well face the fact that our technology has likely passed the affordability of total health care for everyone. We must also realize that at present there is little concern for economy. Neither provider nor consumer has much incentive to save. We need also to realize that the public's appetite for health care is insatiable as long as someone else pays for it.

Our profession needs to inform the health care planners, if they are not already aware, of the tremendous cost to the system of the last year of life, if they are not already aware. This is probably the most difficult problem to address. When the Hippocratic Oath was written Hippocrates could not have anticipated what exist today.

Too often patients who are fully insured, usually at public expense, express a desire to be hospitalized for tests with no rational indication. Frequently they are sent to different hospitals by different doctors with the same battery of admission tests and x-rays. This is a ridiculous waste that might be prevented by the gateway system.

Finally, national health care will have to be rationed at a low

and affordable level with certain safeguards built into it. Organ transplants, cardiac surgery, much vascular surgery and dialysis to name a few, may have to be limited to a greater extent. Sounds harsh and inhumane? Unfortunately, it is the real world.

Canada has a much broader health coverage than we but cannot afford what they have although theirs consumes a much smaller percentage of their GNP than does ours. They are often criticized because of the time it takes for some conditions to get treated. This is, in itself, a necessary form of rationing. Access to certain expensive and sophisticated means of investigations such as MRIs (common place in the U.S. today) is delayed, another form of rationing.

Ours is the best health care system in the world if you can afford it. Unfortunately, we may not be able to afford it for everyone. □

**W. Moncure Dabney, MD**  
**Editor Emeritus**

### **COMMENTS or QUERIES....**

**The Editors of *Journal MSMA* invite you to comment on any material that appears in or is absent from the publication.**

**If you have a query or comment, please send it to:**

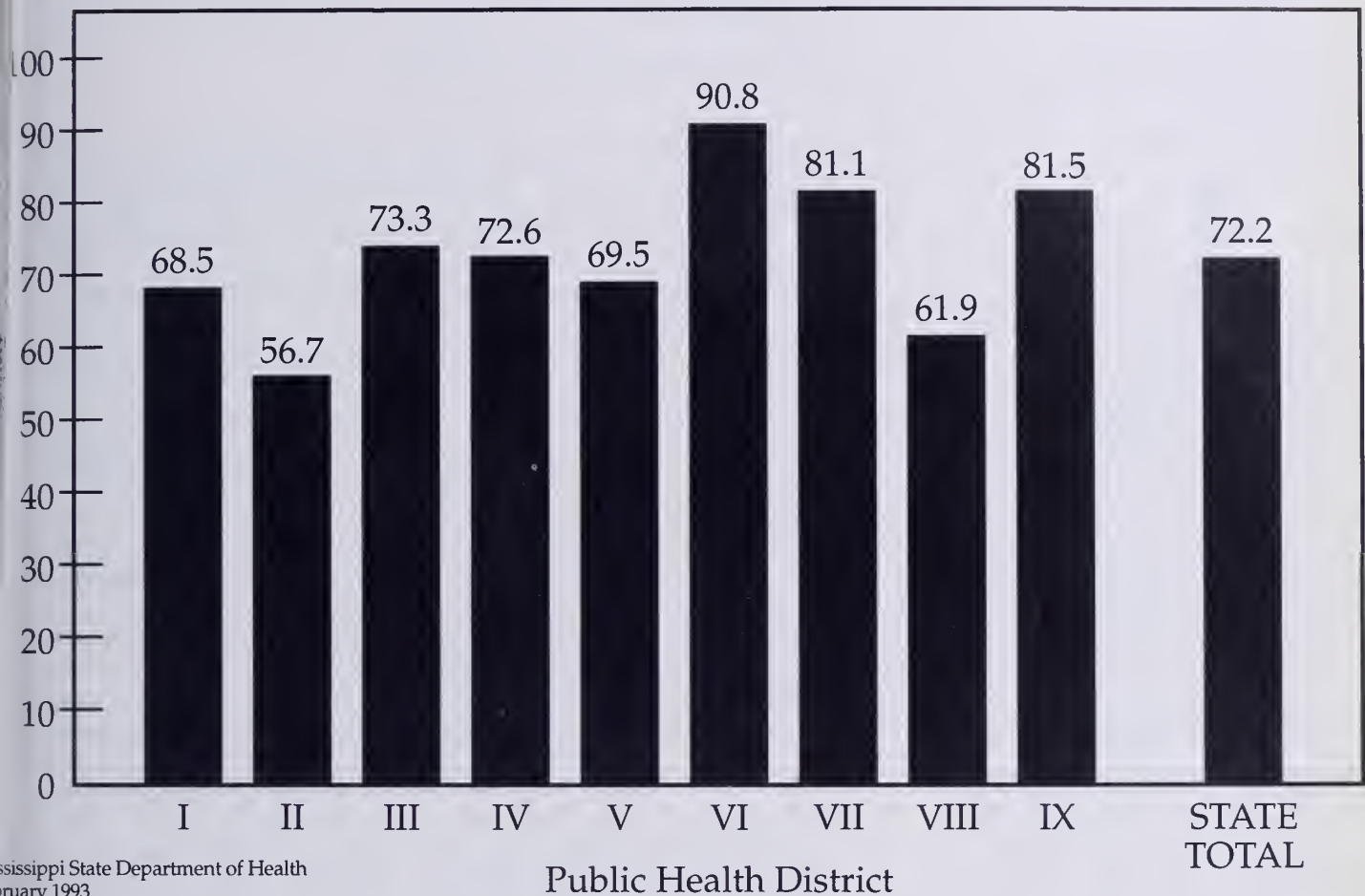
**The Editor,  
*Journal MSMA*,  
PO Box 5229,  
Jackson, MS  
39296-5229**



# Mississippi Immunization Status

1992 Survey Of Two Year Olds

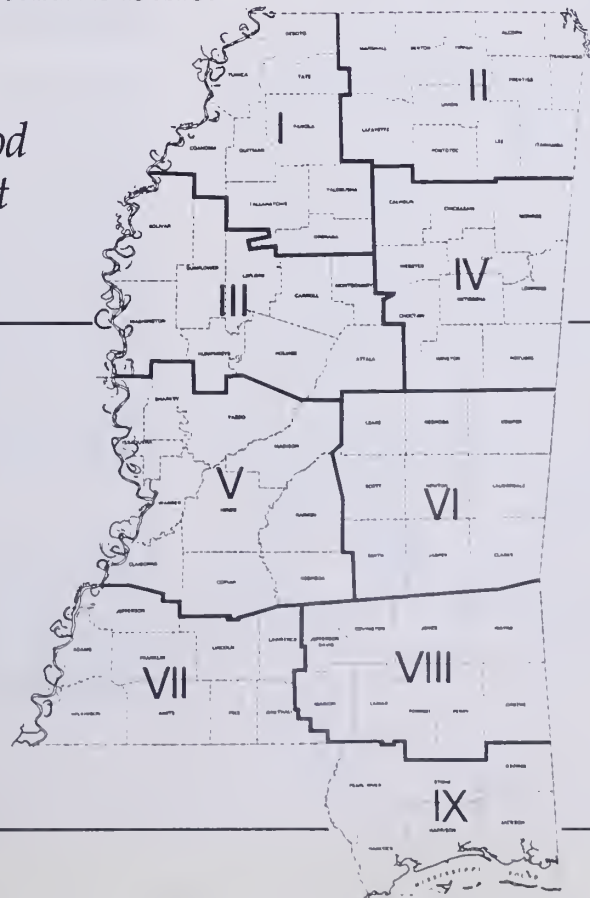
Completion Status By District

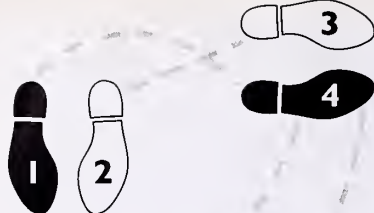


*The Healthy People Year 2000*  
immunization goal is to increase childhood  
immunization levels to at least 90 percent  
of two-year-olds (a 20 percent increase)

## Mississippi State Department of Health Public Health Districts

- Northwest Public Health District I
- Northeast Public Health District II
- Delta Hills Public Health District III
- Tombigbee Public Health District IV
- West Central Public Health District V
- East Central Public Health District VI
- Southwest Public Health District VII
- Southeast Public Health District VIII
- Coastal Plains Public Health District IX





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## Interactions

### Medical Staff

### Leadership Conference on Managing Change

October 1-3, 1993 Naples, Florida

We can't dance around the issue any longer. Health system reform is occurring at a fast pace. And it's going to take some fancy footwork for physicians to maintain autonomy and control within their practices.

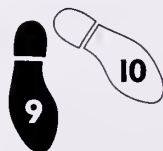
Master the moves that will help you excel in this environment by attending the fourth annual Interactions Medical Staff Leadership Conference: Managing Change. Sponsored by the American Medical Association (AMA), in cooperation with the Medical Association of Georgia and the Florida Medical Association, this comprehensive three-day conference is designed specifically for new and experienced medical staff leaders.

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- Gaining a greater understanding of health policy and medical practice issues
- Acquiring the knowledge and tools to deal with the changes surrounding health system reform

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## COMMENT

### National Vaccine Advisory Committee Standards for Immunization Practice

During the 125th Annual Session a resolution was passed by the MSMA House of Delegates endorsing the National Vaccine Advisory Committee Standards for Immunization Practice. These standards are printed here for your information. On the preceding page of this issue is a graph prepared by the Mississippi State Department of Health showing the immunization status of Mississippi's two-year-olds.

#### STANDARDS FOR PEDIATRIC IMMUNIZATION PRACTICES:

- Standard 1. Immunization services are readily available.
- Standard 2. There are no barriers or unnecessary prerequisites to the receipt of vaccines.
- Standard 3. Immunization services are available free or for a minimal fee.
- Standard 4. Providers utilize all clinical encounters to screen and, when indicated, immunize children.
- Standard 5. Providers educate parents and guardians about immunization in general terms.
- Standard 6. Providers question parents or guardians about contraindications and, before immunizing a child, inform them in specific terms about the risks and benefits of the immunizations their child is to receive.
- Standard 7. Providers follow only true contraindications.
- Standard 8. Providers administer simultaneously all vaccine doses for which a child is eligible at the time of each visit.
- Standard 9. Providers use accurate and complete recording procedures.
- Standard 10. Providers co-schedule immunization appointments in conjunction with appointments for other child health services.
- Standard 11. Providers report adverse events following immunization promptly, accurately and completely.
- Standard 12. Providers operate a tracking system.
- Standard 13. Providers adhere to appropriate procedures for vaccine management.
- Standard 14. Providers conduct semi-annual audits to assess immunization coverage levels and to review immunization records in the patient populations they serve.
- Standard 15. Providers maintain up-to-date easily retrievable medical protocols at all locations where vaccines are administered.
- Standard 16. Providers operate with patient-oriented and community-based approaches.
- Standard 17. Vaccines are administered by properly trained individuals.
- Standard 18. Providers receive ongoing-education and training on current immunization recommendations. □



## Dr. Ward Is New Medical Examiner

Dr. Emily Wofford Ward, an Alabama medical examiner and former Jackson resident, has been selected to fill the combined positions of state medical examiner and director of the Mississippi Crime Laboratory.

In announcing Dr. Ward's hiring, Commissioner of Public Safety Jim Ingram said, "As a native Mississippian, Dr. Ward has keen insight into our state's forensic needs and requirements. She has first hand knowledge of Mississippi's coroner system, the law enforcement community, the criminal justice system, the courts and the medical profession." Ingram said. "Her education, training, current employment and reputation provide a strong foundation to enhance the accountability of the crime lab/medical examiner system."

Dr. Ward is leaving the Alabama Department of Forensic Sciences in Mobile, where she is state medical examiner at Mobile's Regional IV Laboratory, covering eight counties. She also is a clinical assistant professor of pathology at the University of South Alabama Medical Center.

She will be the first person to serve in the dual role as medical examiner and Crime Lab director.

Combining the positions would "provided continuity in services and allow for a sharing

of resources which will save funds to be utilized in a more efficient manner," said Commissioner Ingram.

Offices for the medical examiner and Crime Lab are housed together in a 27,000 square foot complex containing the state's first forensic morgue, completed in 1992.

Dr. Ward received a bachelor's degree from Southern Methodist University in Dallas and the MD degree from Jefferson Medical College in Philadelphia, PA.

## Scholarship Endowment Honors Dr. W. H. Parker

Millsaps College has established an endowed scholarship in memory of Dr. W. H. Parker of Heidelberg.

The William H. Parker Endowed Scholarship was set up with initial gifts of \$3,500 from family and friends and will be endowed at \$10,000 over a five-year period.

The scholarship will give preference to pre-med students from Jasper, Jones, Clarke or Wayne counties, but won't be restricted to this area of study or to these geographic regions.

The late Dr. Parker, a 1937 graduate of Millsaps College, served as student body president, president of Lambda Chi Alpha, and as a member of Omicron Delta

Additionally, she has completed post-graduate training in general surgery at Thomas Jefferson University Hospital in anatomic and clinical pathology at the University of Mississippi Medical Center and in forensic pathology at the University of Alabama.

She is certified in anatomic and clinical pathology and forensic pathology by the American Board of Pathology.

She is the daughter of Dr. and Mrs. John Woffard of Jackson. □

Kappa and Eta Sigma. He moved to Heidelberg in 1947 after serving in the U. S. Army Medical Corps during World War II. He was awarded the Bronze Medal of Honor.

He served as a member of the Heidelberg Board of Alderman for 26 years and was a member of Rotary International. He was also a member of the American Medical Association, Mississippi State Medical Association and the South Mississippi Medical Society.

Gifts to the Dr. W. H. Parker Endowed Scholarship Fund may be sent to Millsaps College, P.O. Box 150552, Jackson, MS 39210-0001. □

## Seven Mississippi Physicians Appointed Cancer Liaisons

Seven Mississippi physicians have received a three-year appointment as Cancer Liaison Physician for their local hospital's cancer program. They are: **Dr. C. Ron Cannon, MD, FACS**, of Flowood, Rankin Medical Center; **J. Robert Coltharp, Jr, MD, FACS**, of Hattiesburg, Methodist Hospital; **Larry H. Day, MD, FACS**, of Hattiesburg, Forrest General Hospital; **Larry J. Fontenelle, MD, FACS**, of Biloxi, VA Medical Center; **Wyatt C. Fowler, MD**, of Keesler AFB, US Air Force Medical Center; **Michael H. Lovelace, MD, FACS**, of Oxford, Baptist Memorial Hospital and **Robert P.**

**Mathis, MD, FACS**, of Tupelo, North Mississippi Medical Center.

The Cancer Liaison Program is an integral part of the Commission on Cancer of the American College of Surgeons. These physicians are among a national network of over 2,000 volunteer Cancer Liaison Physicians who provide leadership and support to the Approvals Program, and other Commission on Cancer Activities. Established in 1956, the Commission on Cancer, which is composed of Fellows of the College and liaison members representing 30 other cancer-related organizations, has approved more than 1,300 cancer program facilities across the country. The Commission reviews each institution's cancer program for conformity to high standards set by the Commission, and encour-

ages participating hospitals to equip and staff themselves so that they are able to provide the best in the diagnosis and treatment of cancer.

An integral part of an approved cancer program is its cancer registry. All patients who are diagnosed as having cancer or are being treated for the disease are listed in the registry so that the hospital can maintain contact with them and make sure that they receive continuing care and assistance with rehabilitation. Information collected through the registry allows hospitals to participate in national studies that are designed to improve patient care. Each year since 1976, more than 800 hospital cancer programs have collaborated with the Commission on these studies. □

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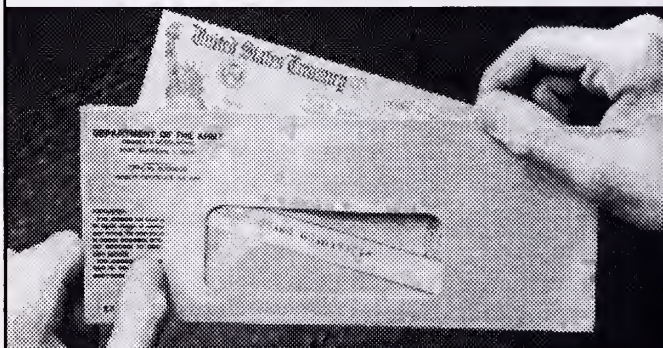
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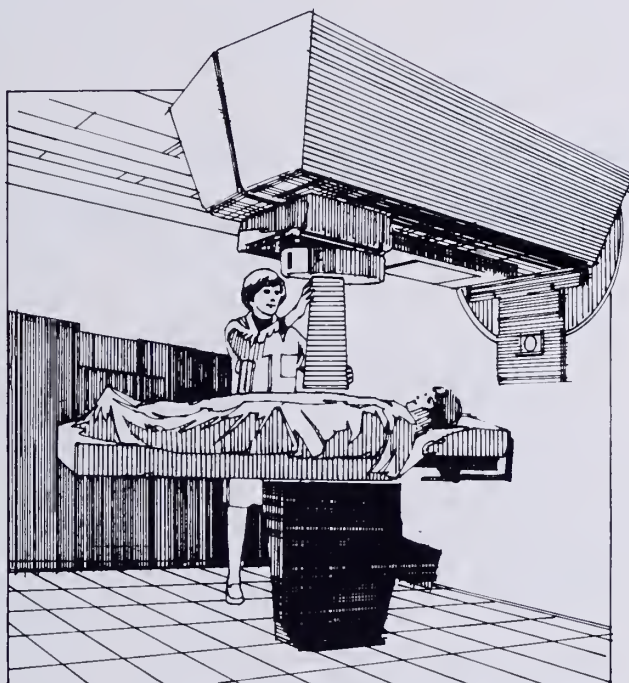


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# For Your Benefit

## First lady asks for physician input to ensure meaningful reform

Hillary Rodham Clinton pushed all the right buttons at the AMA Annual Meeting -- a strong indication of the Association's success in influencing the outcome of the president's reform proposal.

"Her appearance is testimony to her understanding of the critical role physicians will play if system reform is to succeed," said AMA Executive Vice President James S. Todd, MD.

In a 50-minute speech to the AMA's House of Delegates, Mrs. Clinton asked the Association to continue its input into the White House workings on reforming the health system. In return, she promised relief from administrative hassles, limits on malpractice suits, and release of utilization review and "government second guessing of medical decisions."

Mrs. Clinton praised the Association for its extensive input into the reform process.

"I am deeply grateful on a personal level that members of the AMA leadership spent invaluable time coming to meeting after meeting, day after day, sharing their ideas, reacting to ideas at the White House," she said. "And of course, in the course of that, we learned we had many common goals and objectives."

These common interests were notably similar to those in Health Access America, the AMA's reform proposal. She promised universal coverage, a comprehensive benefits package, community rating and free choice.

"We will have not just choice for patients as to which plan they choose to join, but choice for physicians as to which plan they choose to practice with, including the option of being part of more than one plan at the same time."

She sympathized with physicians over government bureaucracy, saying, "We have to simplify and eliminate the burden from regulation created under CLIA." She also said the plan will "offer a serious proposal to curb malpractice problems."

AMA Trustee Nancy W. Dickey, MD, summed up the first lady's speech by saying, "She held out a hand in partnership."

Once the president's plan is unveiled sometime within the next several months, Dr. Todd said the AMA will not take a position until it has an opportunity to see the specifics of the proposal.

The Association will conduct an all-physician mailing giving a detailed AMA analysis of the plan after it is released.



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## Physicians: Time to take action

Physicians, as individuals and as a group, can play a key role in health system reform. Efforts of organized medicine will be tested as never before. Your medical society is the best place to start. It will already have plans to respond to the Clinton plan. Your society will identify key state and federal representatives. And it will provide information on political positions, voting records and office addresses. Here are some suggestions from the AMA:

- *Stay informed.* Shortly after the release of the Clinton plan, you will receive a comprehensive summary and analysis from the AMA. The summary will include the implications of the

Clinton plan for your practice and your patients.

- *Know your elected officials.* Establish a relationship with your senators and representatives. Introduce yourself as a physician and a constituent. Write to them or fax your messages. Ask to meet to discuss health reform issues and what it means to your patients. To telephone senators and representatives in Washington, D.C., call (202) 224-3121. Ask for your senator or representative by name.

- *Get your message across.* Use your own words and experiences. Caring for people is what health system reform is all about.

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## AMA-led campaign opposes enterprise liability

The Clinton administration reportedly has backed away from its intention to propose enterprise liability, after an AMA-led campaign advised that the profession would not consider it an "acceptable alternative" to real tort reform.

The AMA joined with specialty and state medical societies to shift the debate back to serious tort reform.

"We are pleased that the administration is reportedly considering reforms that

include limits on awards for non-economic damages and attorneys' fees. Legal fees and administrative costs eat up 60 percent of patient compensation," said AMA Executive Vice President James S. Todd, MD.

Real tort reform fairly compensates injured patients, reduces costs, eliminates windfall judgments, and assures quality care. It also caps non-economic damages, limits lawyers' fees and staggers large awards.

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## AMA success: IRS withdraws qualifying rules

IRS' withdrawal of potentially troubling proposed pension rules is a significant AMA regulatory victory; this comes as the result of AMA coalition lobbying and legal work done jointly with several national specialty societies during the past three years.

The proposal could have created enormous pension qualification problems for hospital-based physicians

by requiring them to provide pension plans for hospital staff under their clinical supervision.


IRS' action means that hospital-based physicians who clinically supervise hospital staff cannot be fined for not providing pension arrangements, nor must they dismantle their existing pension plans.

# AMA 1993 ANNUAL MEETING




 Delegates and Alternate Delegates to the AMA, from left: J. Elmer Nix, MD, Jackson; Fred L. McMillan, MD, Jackson; Alton B. Cobb, MD, Jackson and William C. Gates, MD, Columbus.





 Don Q. Mitchell, MD, left, is M. President and a Delegate to the A. James C. Waites, MD of Laurel, right, a Delegate to the AMA.



 W. Joseph Burnett, MD, Oxford, Delegate to the AMA, front; Dewitt G. Crawford, MD, center, District 5 Representative MSMA Board of Trustees and Eric E. Lindstrom, MD, Laurel, rear, District 6 Representative MSMA Board of Trustees.



 Sidney O. Graves, MD, of Natchez is immediate past chairman of the Southeastern States Delegation.

 George E. McGee, MD, of Hattiesburg, left, is a member of the AMA Council on Long Range Planning and Development. Dewitt G. Crawford, MD, of Louisville, center, and J. Edward Hill, MD, of Hollandale, right, is a member of the AMA Council on Legislation.







Kathy Gersh, right, of Hattiesburg accepted the AMA Alliance HAP Award on behalf of South Mississippi Medical Auxiliary. Peggy Crawford, of Louisville, center, is president of the MSMA Alliance and Jeannie Morrison, of Hattiesburg, left, is MSMAA Health Projects Chairman.



Lamar Weems, MD, of Jackson, left, served on AMA Reference Committee C.



Candace E. Keller, MD, of Hattiesburg, right, is a member of the AMA Women in Medicine Advisory Panel. William A. Spencer, MD, left, of Oxford is District 2 Representative, MSMA Board of Trustees.



Julian C. Henderson, MD, of Jackson, right, District 4 Representative, MSMA Board of Trustees and his wife Merle, left.



Faser Triplett, MD of Jackson was a candidate for the AMA Board of Trustees at the June meeting.



*Mississippi Medical Auxiliary Members attending the June AMA Alliance Annual Meeting were: seated from left, MSMAA President-elect Karen Stephens, Hattiesburg; MSMAA President Peggy Crawford, Louisville; MSMAA Immediate Past President Kathy*



*Carmichael, Hattiesburg. Standing from left, MSMAA Treasurer Jane Ladner, Jackson; Nancy Lindstrom, Laurel AMA Alliance Legislative Committee Member; Merrell Rogers, Tupelo, AMA Alliance Membership Committee Member, Cathy Gersh, Hattiesburg, Immediate Past President South Mississippi Medical Auxiliary; MSMAA Third Vice President Peggy Sprabery, Pascagoula; and MSMAA Second Vice President Jeanne Morrison, Hattiesburg. □*

## Hattiesburg Project Wins National Health Award

The South Mississippi Medical Auxiliary of Hattiesburg was honored in June when the American Medical Association Alliance presented the 1993 Health Awareness Promotion (HAP) Awards at its annual meeting in Chicago, IL.

HAP Awards were presented in three separate categories, and the Hattiesburg auxiliary's Domestic Abuse Transitional Home competed with more than 40 other submissions for the "auxiliary sponsored health education program or action project." 1992-93 AMA Auxiliary President Priscilla Gerber, left, commended Hattiesburg President Cathy Gersh, right, and presented her with a plaque.

The award culminates more than a year's efforts to find, fund, and furnish the domestic abuse shelter,

and physicians.

Large enough to accommodate three to four families, the home will serve as a refuge in which women who have been abused can re-established themselves in the community. With ongoing support from the auxiliary, the shelter will be operated by the Domestic Abuse Family Center based in Laurel, Mississippi and will offer a full victim assistance program including psychological counseling and economic assistance.

The efforts of the auxiliary earned press coverage from a variety of local newspapers and television stations, and will be featured in the November issue of FACETS, the Alliance Magazine. □



for which the auxiliary raised \$30,000 with donations from local organizations, the medical society, various fund-raising efforts,



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## Faculty Promotions

Twenty-eight faculty members in the Schools of Medicine, Nursing and Health Related Professions have received promotions at the University of Mississippi Medical Center.

UMC vice chancellor Dr. Norman C. Nelson announced the promotions, effective July 1, following approval by the Board of Trustees of State Institutions of Higher Learning.

Promoted to the rank of professor in the medical school were **Dr. Bernard I. Blumenthal**, **Dr. Phillip E. Cranston** and **Dr. James U. Morano** (radiology), **Dr. Ching-Jygh Chen** (ophthalmology), **Dr. James L. Griffith** (psychiatry and human behavior), **Dr. Bobby J. Heath** and **Dr. Galen V. Poole** (surgery), **Dr. Rathi V. Iyer**, **Dr. George W. Moll Jr.**, and **Dr. Paul H. Parker** (pediatrics), **Dr. Anastasios S. Mihas** and **Dr. Ralph B. Vance** (medicine). Medical school faculty appointed to associate professor included **Dr. John D. Current** and **Dr. Kerri M. Robertson** (anesthesiology), **Dr. J. David Dickman** and **Dr. James E. Peck** (surgery), **Dr. Glen R. Graves** and **Dr. John E. Moffitt** (pediatrics), **Dr. Ronald J. Kendig** (orthopedics), **Dr. Thomas J. Payne** (psychiatry and human behavior) and **Dr. Cynthia I. Powers** (radiology).

Centerwide faculty who were

promoted to associate professor were **Dr. S.G.P. Hardy** and **Dr. Susan Warren** (anatomy), **Dr. Robert L. Hester** (physiology and biophysics) and **Dr. Mona T. Norcum** (biochemistry).

**Dr. Sharon Lobert** in the School of Nursing was promoted to associate professor, and **Ann Peden** (health information management) and **Dolph Woodall** (physical therapy) rose to the rank of associate professor in the School of Health Related Professions.

**Dr. Blumenthal** is director of pediatric radiology and has been a member of the faculty since 1973. He holds both the MD and the master of science (in microbiology) from UMC. He took residency training at the Graduate Hospital of the University of Pennsylvania.

**Dr. Cranston** directs computerized tomography (CT) in the radiology. He earned the MD at UMC and completed residency training here. He was on the faculty from 1974-1976 and since 1978.

**Dr. Morano** directs the residency program in radiology and the special procedures division. He earned the MD and completed residency training at UMC. He was on the faculty from 1982-1983 and since 1984.

**Dr. Chen** directs retinal services and research in the ophthalmology department. He completed medical training and ophthalmology residency training in

Taipei, Taiwan. He completed a retinal fellowship and was chief resident in ophthalmology at Cook County Hospital, the University of Chicago. He has been a member of the faculty since 1979.

**Dr. Griffith** directs the family therapy program in the psychiatry department and is medical director of the behavioral medicine unit and the sleep disorders center. Board certified in neurology and psychiatry, he completed a neurology residency here and a psychiatry residency at Massachusetts General Hospital in Boston where he was also chief resident. He joined the UMC faculty in 1985.

**Dr. Heath** is chief of cardiothoracic surgery and program director for the cardiothoracic surgery residency. A member of the faculty since 1978, he earned the MD at UMC and completed residency training here.

**Dr. Poole**, a faculty member since 1989, directs the trauma service. A graduate of the University of Kentucky College of Medicine, he completed internship, residency training and a fellowship in surgical research at Wake Forest University and Bowman Gray School of Medicine.

**Dr. Rathi Iyer** directs the hemophilia and sickle cell programs in the Division of Pediatric Hematology-oncology. A UMC faculty member since



## Dr. Nelson To Retire In 1994

1973, she earned her medical degree at the Ghandi Medical College of Osmania University, completed residency training at Detroit General Hospital and fellowship in pediatric hematology and oncology at the Children's Hospital of Michigan in Detroit.

Dr. Moll, director of pediatric endocrinology since 1987, holds the PhD and MD from the University of Chicago. He completed pediatric residency training at the University of Michigan Mott Children's Hospital in Ann Arbor and a pediatric endocrinology fellowship at Wyler Children's Hospital, University of Chicago.

Dr. Parker earned the MD and completed residency training at UMC. He completed a fellowship in pediatric gastroenterology at Vanderbilt University Hospital in Nashville in 1981 and joined the UMC faculty to direct the pediatric gastroenterology division.

Dr. Mihas, staff gastroenterologist at the Department of Veterans Affairs Medical Center and member of the UMC faculty since 1988, completed his medical training at the University of Athens Medical School in Greece. He completed a research fellowship at Harvard Medical School and a fellowship in gastroenterology at the University of Alabama in Birmingham.

Dr. Vance has been a member of the UMC faculty since 1978 when he completed a fellowship in hematology-oncology at UMC. He earned his MD at UMC and completed residency training here. □

Chancellor R. Gerald Turner announced to the Board of Trustees of State Institutions of Higher Learning and the UMC faculty that Dr. Norman C. Nelson, vice chancellor for health affairs and dean of the School of Medicine, plans to retire in August, 1994.

Dr. Nelson has been the Medical Center's chief executive officer since July 15, 1973. He has the longest tenure of any academic health sciences center CEO in the country.

"Dr. Nelson's dedicated and energetic leadership of the Medical Center and his commitment

to its mission is state higher education have enabled the institution to make truly dynamic progress in the past two decades," Chancellor Turner said.

Chancellor Turner has appointed Dr. Winfred L. Wiser, professor of obstetrics and gynecology and chairman of the department, to chair the University search committee which will identify and recommend a successor to Dr. Nelson. Dr. Les Wyatt, vice chancellor for executive affairs at the University of Mississippi, will co-chair the committee.

If you have nominations please send them to Dr. Wiser at UMC. □

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**Orlando J. Andy, Jr.**, has associated with the Hattiesburg Clinic in the practice of general surgery, 415 South 28th Avenue, Hattiesburg.

**Woodrow W. Brand, III**, announces the opening of his medical practice of general surgery, peripheral vascular surgery laparoscopic surgery, Professional Building, 303 Second Avenue North, Amory.

**William C. Brawner** has associated with Joseph J. Chappell, Jr., MD, in the medical and surgical practice of Ophthalmology, Tupelo

Eye Clinic, Satellite Office, 502 E. Eason Boulevard, Tupelo.

**Harry Butler and Glen Smith** of Hattiesburg are pleased to announce the relocation of The Hematology & Oncology Clinic to 103 Asbury Circle, Methodist Medical Park, Hattiesburg.

**Susan Buttross** of Madison was recently elected president of the Mississippi Chapter of the American Academy of Pediatrics.

**Robert W. Calcote**, announces the relocation and opening of his

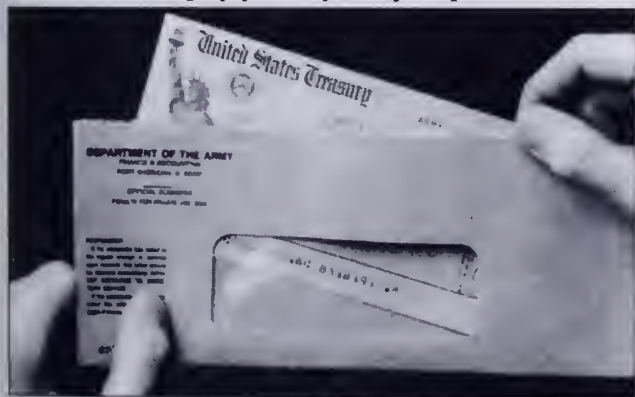
practice in Auburn, Alabama and announces the arrival of Gary G. Bolton in the practice of Dermatology, 764 Lakeland Drive #408, Jackson.

**William Larkin Carter, III**, has associated with the Radiological Group, PA, 1405 North State Street, Jackson, for the practice of Diagnostic Radiology.

**John W. Cook**, has associated with The Jackson Clinic For Women, PA for the practice of Obstetrics and Gynecology, 1030 North Flowood Drive, Jackson.

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**Lee B. Drake**, has associated with Physicians and Surgeons Clinic, for the practice of obstetrics and gynecology in Amory.

**Parker Ellison** has associated with the Children's Medical Group, P. A. for the practice of pediatrics, 800 Carlisle, Jackson.

**R. J. Field, Jr.**, of the Field Clinic and Field Hospital, Centreville, MS, attended the quarterly meeting of the Board of Regents of the American College of Surgeons in Chicago, June 10-12. He was the banquet speaker and spoke on the topic *A Visit to Centreville -- The Center of the Universe*.

**Joseph C. Hillman, Jr.**, announces the relocation of his medical practice to the Lowndes Family Medical Clinic, 824, Alabama

Street, Columbus, MS.

**L. G. Hopkins** of Oxford recently received a Distinguished Service in Aging Award from the Division of Aging and Adult Services for freely giving his time and expertise to improve the lives of Mississippi's elderly citizens.

**Stephen Johnson** has associated with Internal Medicine Clinic of Laurel, in the practice of gastroenterology.

**McKinley S. Lundy** has associated with MEA Medical Clinics, Jackson in the specialty of occupational and environmental medicine.

**Thomas P. Mills** has associated with **Walter T. Boone**, and **Roland F. Garretson, Jr.**, in the Digestive Disease Clinic, for the practice of

Gastroenterology.

**Beverly Myers** of Gulfport announces the relocation of her medical practice of reumatology to Hattiesburg in association with **Chris H. Benson**, and **James B. Pennebaker** with the Arthritis Center of Mississippi, Hattiesburg

**John H. McVey, Sr.**, of Jackson announces the relocation of his office for the practice of ophthalmology, pediatric ophthalmology, and adult strabismus to Medical Arts East, 1190 North State Street suite, 203, Jackson.

**William Mark Molpus** has joined the Hattiesburg Radiology Group in the practice of Diagnostic Radiology with fellowship training in Neuroradiology.

## Physicians' Recognition Award



Four MSMA members were named recipients of the AMA Physicians Recognition Award in June 1993. This award is presented by the American Medical Association to Physicians who have voluntarily completed a specified number of continuing medical education hours. These individuals are presented below by Medical Society.

CENTRAL MEDICAL SOCIETY  
**David Kyle Ball, MD**

PRAIRIE MEDICAL SOCIETY  
**Chester C. Lott, MD**

DELTA MEDICAL SOCIETY  
**Frank McVey Tilton, MD**

SINGING RIVER MEDICAL SOCIETY  
**Michael D. Horowitz, MD**

Applications for the AMA Physicians Recognition award can be obtained at any time by writing or calling the AMA Office of Physician Credentials and Qualifications: (312) 464-4672.



**Paul Moore**, of Pascagoula, Medical Director of the Singing River Hospital Radiology Department, was recently honored with a reception marking his 30th year with the hospital.

**Rhonda Henderson Powell** has associated with East Lakeland OB-GYN Associates, P.A. for the practice of obstetrics and gynecology, 1020 River Oaks Drive, Suite, 320, Jackson.

**Mark S. Puricelli** has associated with the Hattiesburg Clinic in the practice of neurology, 415 South 28th Avenue, Hattiesburg.

**W. Ray Reed, Jr.**, has associated with Radiology of Tupelo, P.A. for the practice of radiation oncology, 990 South Madison, Suite 1, Tupelo.

**David M. Slife**, a cardiologistspecializing in both general and interventional cardiology has joined the Rush Medical Group, P. A. of Meridian.

**David W. Sullivan** has associated with Hinds Internal Medicine Clinic, P.A. for the practice of internal medicine at 1983 McDowell Road, Jackson.

**Joseph R. Terracina**, has associated with John A. Marascalco, for the practice of dermatology-disease of the skin, 1504 Hospital Street, Greenville.

**D. Winn Walcott** has associated with Mississippi Asthma and Allergy Clinic, P.A. for the diagnosis and treatment of asthma and allergic disease, 940 North State Street, Jackson.

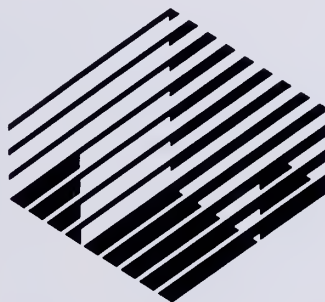
**Benjamin F. Walton** has associated with Rush Medical Group, P. A. for the practice of pulmonary medicine and critical care medicine, Meridian.

**Richard L. Yelverton, Jr.**, has associated with Lakeland Surgical Clinic in the practice of General, Thoracic and Breast Surgery, 971 Lakeland Drive, Suite 1460, Jackson. □

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Olive Branch/Pearl/Petalatche/Petal/Richland/Ridgeland/Southaven  
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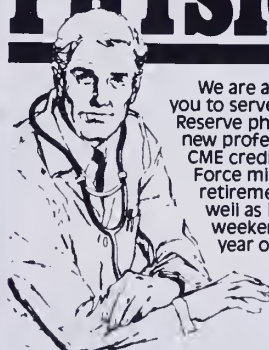
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## Index to Advertisers

Bristol-Myers Squibb Company -  
Pravachol ..... third and fourth cover

Cambridge Equity Advisors ..... 266  
CancerPay Plus ..... 283  
CompHealth ..... 297

Disability Determination ..... 296

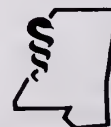
Eli Lilly & Co. - Humulin ..... 2

Medical Assurance Co. of MS ..... 292  
Medley and Company ..... 298  
MS Emergency Association ..... 297  
MS Physicians Insurance Company ..... 289  
MSMA Benefit Plan & Trust ..... 273

Premier Printing ..... 291

The Doctors' Company ..... 4  
Trustmark ..... 295

US Air Force ..... 272  
US Air Force Reserve ..... 297  
US Army Active ..... 282  
US Army Reserve ..... 293





**reference:** 1. Jones PH, et al. Once-daily pravastatin in patients with primary hypercholesterolemia: a dose-response study. *Clin Cardiol.* 1991;14:146-151.

## RAWACHOL® (Pravastatin Sodium Tablets)

### CONTRAINDICATIONS

hypersensitivity to any component of this medication.

Active liver disease or unexplained, persistent elevations in liver function tests (see WARNINGS).

**Pregnancy and lactation.** Atherosclerosis is a chronic process and discontinuation of lipid-lowering drugs during pregnancy should have little impact on the outcome of long-term therapy of primary hypercholesterolemia. Cholesterol and other products of cholesterol biosynthesis are essential components for fetal development (including synthesis of steroids and cell membranes). Since HMG-CoA reductase inhibitors decrease cholesterol synthesis and possibly the synthesis of other biologically active substances derived from cholesterol, they may cause fetal harm when administered to pregnant women. Therefore, HMG-CoA reductase inhibitors are contraindicated during pregnancy and in nursing mothers. **Pravastatin should be administered to women of childbearing age only when such patients are highly unlikely to conceive and have been informed of the potential hazards.** If the patient becomes pregnant while taking this class of drug, therapy should be discontinued and the latent appraisal of the potential hazard to the fetus.

### WARNINGS

**Liver Enzymes:** HMG-CoA reductase inhibitors, like some other lipid-lowering therapies, have been associated with biochemical abnormalities of liver function. Increases of serum transaminase (ALT, AST) values to more than 3 times the upper limit of normal occurring on 2 or more (not necessarily sequential) occasions have been reported in 1.3% of patients treated with pravastatin in the U.S. over an average period of 18 months. These abnormalities were not associated with cholestasis and did not appear to be related to treatment duration. In those patients in whom these abnormalities were believed to be related to pravastatin and who were discontinued from therapy, the transaminase levels usually fell slowly to pretreatment levels. These biochemical findings are usually asymptomatic although worldwide experience indicates that anorexia, weakness, and/or abdominal pain may also be present in some patients.

As with other lipid-lowering agents, liver function tests should be performed during therapy with pravastatin. Serum aminotransferases, including ALT (SGPT), should be monitored before treatment begins, every six weeks for the first three months, every eight weeks during the remainder of the first year, and periodically thereafter (e.g., at about six-month intervals). Special attention should be given to patients who develop increased transaminase levels. Liver function tests should be repeated to confirm an elevation and subsequently monitored at more frequent intervals. If increases in AST and ALT equal or exceed three times the upper limit of normal and persist, then therapy should be discontinued. Persistence of significant aminotransferase elevations following discontinuation of therapy may warrant consideration of liver biopsy.

Active liver disease or unexplained transaminase elevations are contraindications to the use of pravastatin (see CONTRAINDICATIONS). Caution should be exercised when pravastatin is administered to patients with a history of liver disease or heavy alcohol ingestion (see CLINICAL PHARMACOLOGY: Pharmacokinetics/Metabolism). Such patients should be closely monitored, started at the lower end of the recommended dosing range, and titrated to the desired therapeutic effect.

**Skeletal Muscle:** Rhabdomyolysis with renal dysfunction secondary to myoglobinuria has been reported with pravastatin and other drugs in this class. Uncomplicated myalgia has also been reported in pravastatin-treated patients (see ADVERSE REACTIONS). Myopathy, defined as muscle aching or muscle weakness in conjunction with increases in creatine phosphokinase (CPK) values to greater than 10 times the upper limit of normal was reported to be possibly due to pravastatin in only one patient in clinical trials (<0.1%). Myopathy should be considered in any patient with diffuse myalgias, muscle tenderness or weakness, and/or marked elevation of CPK. Patients should be advised to report promptly unexplained muscle pain, tenderness or weakness, particularly if accompanied by malaise or fever. **Pravastatin therapy should be discontinued if markedly elevated CPK levels occur or myopathy is diagnosed or suspected. Pravastatin therapy should also be temporarily withheld in any patient experiencing an acute or serious condition predisposing to the development of renal failure secondary to rhabdomyolysis, e.g., sepsis; hypotension; major surgery; trauma; severe metabolic, endocrine, or electrolyte disorders; or uncontrolled epilepsy.**

The risk of myopathy during treatment with lovastatin is increased if therapy with either cyclosporine, gemfibrozil, erythromycin, or niacin is administered concurrently. There is no experience with the use of pravastatin together with cyclosporine. Myopathy has not been observed in clinical trials involving small numbers of patients who were treated with pravastatin together with niacin. One trial of limited size involving combined therapy with pravastatin and gemfibrozil showed a trend toward more frequent CPK elevations and patient withdrawals due to musculoskeletal symptoms in the group receiving combined treatment as compared with the groups receiving placebo, gemfibrozil, or pravastatin monotherapy. Myopathy was not reported in this trial (see PRECAUTIONS: Drug Interactions). One patient developed myopathy when clofibrate was added to a previously well tolerated regimen of pravastatin; the myopathy resolved when clofibrate therapy was stopped and pravastatin treatment continued. **The use of fibrates alone may occasionally be associated with myopathy. The combined use of pravastatin and fibrates should generally be avoided.**

### PRECAUTIONS

**General:** Pravastatin may elevate creatine phosphokinase and transaminase levels (see ADVERSE REACTIONS). This should be considered in the differential diagnosis of chest pain in a patient on therapy with pravastatin.

**Homozygous Familial Hypercholesterolemia.** Pravastatin has not been evaluated in patients with rare homozygous familial hypercholesterolemia. In this group of patients, it has been reported that HMG-CoA reductase inhibitors are less effective because the patients lack functional LDL receptors.

**Renal Insufficiency.** A single 20 mg oral dose of pravastatin was administered to 24 patients with varying degrees of renal impairment (as determined by creatinine clearance). No effect was observed on the pharmacokinetics of pravastatin or its 3 $\alpha$ -hydroxy isomeric metabolite (SQ 31,906). A small increase was seen in mean AUC values and half-life (t<sub>1/2</sub>) for the inactive enzymatic ring hydroxylation metabolite (SQ 31,945). Given this small sample size, the dosage administered, and the degree of individual variability, patients with renal impairment who are receiving pravastatin should be closely monitored.

**Information for Patients:** Patients should be advised to report promptly unexplained muscle pain, tenderness or weakness, particularly if accompanied by malaise or fever.

**Drug Interactions:** Immunosuppressive Drugs, Gemfibrozil, Niacin (Nicotinic Acid), Erythromycin. See WARNINGS: Skeletal Muscle.

**Antipyrine:** Clearance by the cytochrome P450 system was unaltered by concomitant administration of pravastatin. Since pravastatin does not appear to induce hepatic drug-metabolizing enzymes, it is not expected that any significant interaction of pravastatin with other drugs (e.g., phenytoin, quinidine) metabolized by the cytochrome P450 system will occur.

**Cholestyramine/Colestipol:** Concomitant administration resulted in an approximately 40 to 50% decrease in the mean AUC of pravastatin. However, when pravastatin was administered 1 hour before or 4 hours after cholestyramine or 1 hour before colestipol and a standard meal, there was no clinically significant decrease in bioavailability or therapeutic effect. (See DOSAGE AND ADMINISTRATION: Concomitant Therapy.)

**Warfarin:** In a study involving 10 healthy male subjects given pravastatin and warfarin concomitantly for 6 days, bioavailability parameters at steady state for pravastatin (parent compound) were not altered. Pravastatin did not alter the plasma protein-binding of warfarin. Concomitant dosing did increase the AUC and C<sub>max</sub> of warfarin but did not produce any changes in its anticoagulant action (i.e., no increase was seen in mean prothrombin time after 6 days of concomitant therapy). However, bleeding and extreme prolongation of prothrombin time has been reported with other drugs in this class. Patients receiving warfarin-type anticoagulants should have their prothrombin times closely monitored when pravastatin is initiated or the dosage of pravastatin is changed.

**Cimetidine:** The AUC<sub>0-12h</sub> for pravastatin when given with cimetidine was not significantly different from the AUC for pravastatin when given alone. A significant difference was observed between the AUC's for pravastatin when given with cimetidine compared to when administered with antacid.

**Digoxin:** In a crossover trial involving 18 healthy male subjects given pravastatin and digoxin concurrently for 9 days, the bioavailability parameters of digoxin were not affected. The AUC of pravastatin tended to increase, but the overall bioavailability of pravastatin plus its metabolites SQ 31,906 and SQ 31,945 was not altered.

**Gemfibrozil:** In a crossover study in 20 healthy male volunteers given concomitant single doses of pravastatin and gemfibrozil, there was a significant decrease in urinary excretion and protein binding of pravastatin. In addition, there was a significant increase in AUC, C<sub>max</sub>, and T<sub>max</sub> for the pravastatin metabolite SQ 31,906. Combination therapy with pravastatin and gemfibrozil is generally not recommended.

In interaction studies with aspirin, antacids [1 hour prior to PRAVACHOL (pravastatin sodium)], cimetidine, nicotinic acid, or probucol, no statistically significant differences in bioavailability were seen when PRAVACHOL was administered.

**Other Drugs:** During clinical trials, no noticeable drug interactions were reported when PRAVACHOL was added to: diuretics, antihypertensives, digitalis, converting-enzyme inhibitors, calcium channel blockers, beta-blockers, or nitroglycerin.

**Endocrine Function:** HMG-CoA reductase inhibitors interfere with cholesterol synthesis and lower circulating cholesterol levels, and, as such, might theoretically blunt adrenal or gonadal steroid hormone production. Results of clinical trials with pravastatin in males and post-menopausal females were inconsistent with regard to possible effects of the drug on basal steroid hormone levels. In a study of 21 males, the mean testosterone response to human chorionic gonadotropin was significantly reduced (p<0.004) after 16 weeks of treatment with 40 mg of pravastatin. However, the percentage of patients showing a  $\geq$ 50% rise in plasma testosterone after human chorionic gonadotropin stimulation did not change significantly after therapy in these patients. The effects of HMG-CoA reductase inhibitors on spermatogenesis and fertility have not been studied in adequate numbers of patients. The effects, if any, of pravastatin on the pituitary-gonadal axis in pre-menopausal females are unknown. Patients treated with pravastatin who display clinical evidence of endocrine dysfunction should be evaluated appropriately. Caution should also be exercised if an HMG-CoA reductase inhibitor or other agent used to lower cholesterol levels is administered to patients also receiving other drugs (e.g., ketoconazole, spiroglactone, cimetidine) that may diminish the levels or activity of steroid hormones.

**CNS Toxicity:** CNS vascular lesions, characterized by perivascular hemorrhage and edema and mononuclear cell

infiltration of perivascular spaces, were seen in dogs treated with pravastatin at a dose of 25 mg/kg/day, a dose that produced a plasma drug level about 50 times higher than the mean drug level in humans taking 40 mg/day. Similar CNS vascular lesions have been observed with several other drugs in this class.

A chemically similar drug in this class produced optic nerve degeneration (Wallenian degeneration of retinogeniculate fibers) in clinically normal dogs in a dose-dependent fashion starting at 60 mg/kg/day, a dose that produced mean plasma drug levels about 30 times higher than the mean drug level in humans taking the highest recommended dose (as measured by total enzyme inhibitory activity). This same drug also produced vestibulocochlear Wallenian-like degeneration and retinal ganglion cell chromatolysis in dogs treated for 14 weeks at 180 mg/kg/day, a dose which resulted in a mean plasma drug level similar to that seen with the 60 mg/kg/day dose.

**Carcinogenesis, Mutagenesis, Impairment of Fertility:** In a 2-year study in rats fed pravastatin at doses of 10, 30, or 100 mg/kg body weight, there was an increased incidence of hepatocellular carcinomas in males at the highest dose (p<0.01). Although rats were given up to 125 times the human dose (HD) on a mg/kg body weight basis, their serum drug levels were only 6 to 10 times higher than those measured in humans given 40 mg pravastatin as measured by AUC.

The oral administration of 10, 30, or 100 mg/kg (producing plasma drug levels approximately 0.5 to 5.0 times human drug levels at 40 mg) of pravastatin to mice for 22 months resulted in a statistically significant increase in the incidence of malignant lymphomas in treated females when all treatment groups were pooled and compared to controls (p<0.05). The incidence was not dose-related and male mice were not affected.

A chemically similar drug in this class was administered to mice for 72 weeks at 25, 100, and 400 mg/kg body weight, which resulted in mean serum drug levels approximately 3, 15, and 33 times higher than the mean human serum drug concentration (as total inhibitory activity) after a 40 mg oral dose. Liver carcinomas were significantly increased in high-dose females and mid- and high-dose males, with a maximum incidence of 90 percent in males. The incidence of adenomas of the liver was significantly increased in mid- and high-dose females. Drug treatment also significantly increased the incidence of lung adenomas in mid- and high-dose males and females. Adenomas of the eye Harderian gland (a gland of the eye of rodents) were significantly higher in high-dose mice than in controls.

No evidence of mutagenicity was observed *in vitro*, with or without rat-liver metabolic activation, in the following studies: microbial mutagen tests, using mutant strains of *Salmonella typhimurium* or *Escherichia coli*; a forward mutation assay in L5178Y TK + / - mouse lymphoma cells; a chromosomal aberration test in hamster cells; and a gene conversion assay using *Saccharomyces cerevisiae*. In addition, there was no evidence of mutagenicity in either a dominant lethal test in mice or a micronucleus test in mice.

In a study in rats, with daily doses up to 500 mg/kg, pravastatin did not produce any adverse effects on fertility or general reproductive performance. However, in a study with another HMG-CoA reductase inhibitor, there was decreased fertility in male rats treated for 34 weeks at 25 mg/kg body weight, although this effect was not observed in a subsequent fertility study when this same dose was administered for 11 weeks (the entire cycle of spermatogenesis, including epididymal maturation). In rats treated with this same reductase inhibitor at 180 mg/kg/day, seminiferous tubule degeneration (necrosis and loss of spermatogenic epithelium) was observed. Although not seen with pravastatin, two similar drugs in this class caused drug-related testicular atrophy, decreased spermatogenesis, spermatocytic degeneration, and giant cell formation in dogs. The clinical significance of these findings is unclear.

**Pregnancy: Pregnancy Category X:** See CONTRAINDICATIONS.

Safety in pregnant women has not been established. Pravastatin was not teratogenic in rats at doses up to 1000 mg/kg daily or in rabbits at doses of up to 50 mg/kg daily. These doses resulted in 20x (rabbits) or 240x (rats) the human exposure based on surface area (mg/meter<sup>2</sup>). However, in studies with another HMG-CoA reductase inhibitor, skeletal malformations were observed in rats and mice. PRAVACHOL (pravastatin sodium) should be administered to women of child-bearing potential only when such patients are highly unlikely to conceive and have been informed of the potential hazards. If the woman becomes pregnant while taking PRAVACHOL, it should be discontinued and the patient advised again as to the potential hazards to the fetus.

**Nursing Mothers:** A small amount of pravastatin is excreted in human breast milk. Because of the potential for serious adverse reactions in nursing infants, women taking PRAVACHOL should not nurse (see CONTRAINDICATIONS).

**Pediatric Use:** Safety and effectiveness in individuals less than 18 years old have not been established. Hence, treatment in patients less than 18 years old is not recommended at this time. (See also PRECAUTIONS: General.)

### ADVERSE REACTIONS

Pravastatin is generally well tolerated, adverse reactions have usually been mild and transient. In 4-month long placebo-controlled trials, 1.7% of pravastatin-treated patients and 1.2% of placebo-treated patients were discontinued from treatment because of adverse experiences attributed to study drug therapy; this difference was not statistically significant. In long-term studies, the most common reasons for discontinuation were asymptomatic serum transaminase increases and mild, non-specific gastrointestinal complaints. During clinical trials the overall incidence of adverse events in the elderly was not different from the incidence observed in younger patients.

**Adverse Clinical Events:** All adverse clinical events (regardless of attribution) reported in more than 2% of pravastatin-treated patients in the placebo-controlled trials are identified in the table below, also shown are the percentages of patients in whom these medical events were believed to be related or possibly related to the drug.

Body System/Event	All Events %		Events Attributed to Study Drug %	
	Pravastatin (N=900)	Placebo (N=411)	Pravastatin (N=900)	Placebo (N=411)
Cardiovascular				
Cardiac Chest Pain	4.0	3.4	0.1	0.0
Dermatologic				
Rash	4.0*	1.1	1.3	0.9
Gastrointestinal				
Nausea/Vomiting	7.3	7.1	2.9	3.4
Diarrhea	6.2	5.6	2.0	1.9
Abdominal Pain	5.4	6.9	2.0	3.9
Constipation	4.0	7.1	2.4	5.1
Flatulence	3.3	3.6	2.7	3.4
Heartburn	2.9	1.9	2.0	0.7
General				
Fatigue	3.8	3.4	1.9	1.0
Chest Pain	3.7	1.9	0.3	0.2
Influenza	2.4*	0.7	0.0	0.0
Musculoskeletal				
Localized Pain	10.0	9.0	1.4	1.5
Myalgia	2.7	1.0	0.6	0.0
Nervous System				
Headache	6.2	3.9	1.7*	0.2
Dizziness	3.3	3.2	1.0	0.5
Renal/Genitourinary				
Urinary Abnormality	2.4	2.9	0.7	1.2
Respiratory				
Common Cold	7.0	6.3	0.0	0.0
Rhinitis	4.0	4.1	0.1	0.0
Cough	2.6	1.7	0.1	0.0

\*Statistically significantly different from placebo.

The following effects have been reported with drugs in this class:

**Skeletal:** myopathy, rhabdomyolysis.

**Neurological:** dysfunction of certain cranial nerves (including alteration of taste, impairment of extra-ocular movement, facial paresis), tremor, vertigo, memory loss, paresthesia, peripheral neuropathy, peripheral nerve palsy.

**Hypersensitivity Reactions:** An apparent hypersensitivity syndrome has been reported rarely which has included one or more of the following features: anaphylaxis, angioedema, lupus erythematosus-like syndrome, polymyalgia rheumatica, vasculitis, purpura, thrombocytopenia, leukopenia, hemolytic anemia, positive ANA, ESR increase, arthritis, arthralgia, urticaria, asthenia, photosensitivity, fever, chills, flushing, malaise, dyspnea, toxic epidermal necrolysis, erythema multiforme, including Stevens-Johnson syndrome.

**Gastrointestinal:** pancreatitis, hepatitis, including chronic active hepatitis, cholestatic jaundice, fatty change in liver, and, rarely, cirrhosis, fulminant hepatic necrosis, and hepatoma; anorexia, vomiting.

**Reproductive:** gynecomastia, loss of libido, erectile dysfunction.

**Eye:** progression of cataracts (lens opacities), ophthalmoplegia.

**Laboratory Test Abnormalities:** Increases in serum transaminase (ALT, AST) values and CPK have been observed (see WARNINGS).

Transient, asymptomatic eosinophilia has been reported. Eosinophil counts usually returned to normal despite continued therapy. Anemia, thrombocytopenia, and leukopenia have been reported with other HMG-CoA reductase inhibitors.

**Concomitant Therapy:** Pravastatin has been administered concurrently with cholestyramine, colestipol, nicotinic acid, probucol and gemfibrozil. Preliminary data suggest that the addition of either probucol or gemfibrozil to therapy with lovastatin or pravastatin is **not** associated with greater reduction in LDL-cholesterol than that achieved with lovastatin or pravastatin alone. No adverse reactions unique to the combination or in addition to those previously reported for each drug alone have been reported. Myopathy and rhabdomyolysis (with or without acute renal failure) have been reported when another HMG-CoA reductase inhibitor was used in combination with immunosuppressive drugs, gemfibrozil, erythromycin, or lipid-lowering doses of nicotinic acid. Concomitant therapy with HMG-CoA reductase inhibitors and these agents is generally not recommended. (See WARNINGS: Skeletal Muscle and PRECAUTIONS: Drug Interactions.)

### OVERDOSE

There have been no reports of overdoses with pravastatin.

Should an accidental overdose occur, treat symptomatically and institute supportive measures as required.



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Please see CONTRAINDICATIONS, WARNINGS, PRECAUTIONS, and ADVERSE REACTIONS in the brief summary of prescribing information on the adjacent page.



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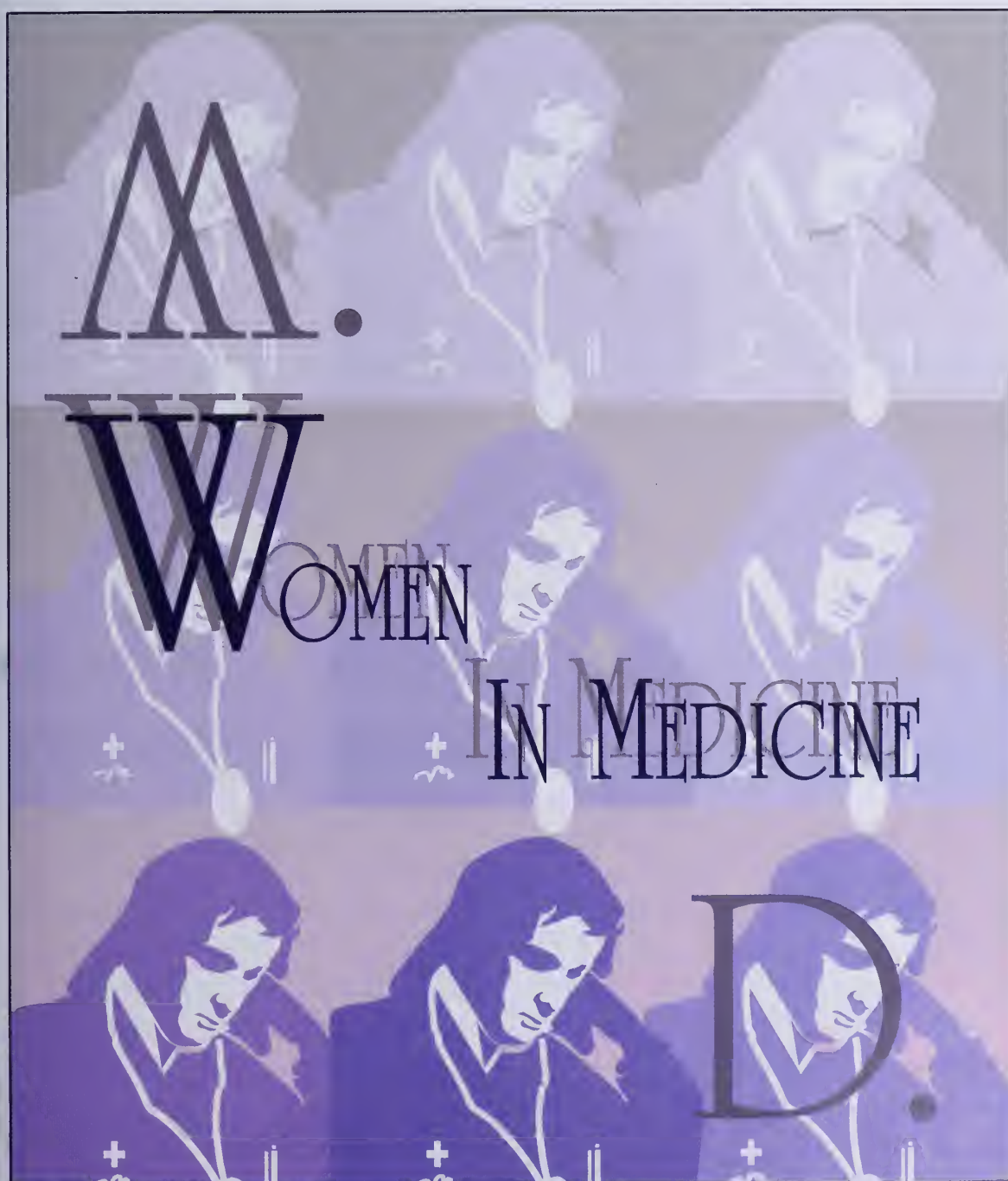


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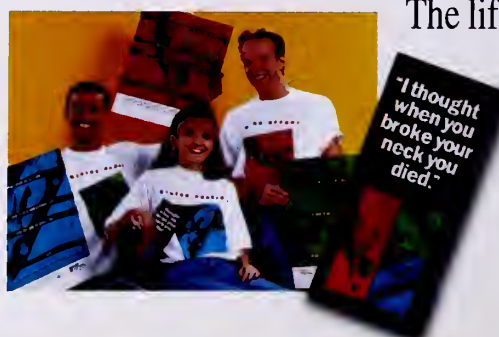
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SEPTEMBER 1993

VOLUME XXXIV

NUMBER 9

## SCIENTIFIC ARTICLES

- The University of Mississippi Medical Center's Antenatal Diagnostic Unit: On The Cutting Edge of Tomorrow** 299  
*William E. Roberts, MD; Kenneth G. Perry, Jr., MD  
Rick W. Martin, MD; John C. Morrison, MD; and  
James N. Martin, Jr., MD*

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## SPECIAL ARTICLE

- Women In Medicine** 306

## EDITORIALS

- United Voices** 312  
*Don Q. Mitchell, MD*  
**Hippocrates Revisited** 313  
*George E. Abraham, MD, Associate Editor*

## DEPARTMENTS

- Comment** 315  
**Medical Organization** 318  
**New Members** 324  
**Deaths** 326  
**Personals** 328  
**Placement Service** 332  
**Classified** 334

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## MS Infant Mortality Rate Edged Slightly Higher

Jackson, MS — Mississippi saw 508 fewer births and 15 more infant deaths last year than in 1991. As a result, the state's infant mortality rate — the number of babies per 1,000 who die before one year of age — rose slightly from 11.4 in 1991 to 11.9 in 1992, according to Mississippi State Department of Health statistics.

State Health Officer Dr. Ed Thompson said that the slight one-year variation is not a statistically significant difference. "The fact that our infant mortality rate has remained essentially level now for several years tells us that the things we've done to reduce it over the past 10 years have done about as much as they're going to do," Dr. Thompson said. "To get the rates down further, we're going to have to do more."

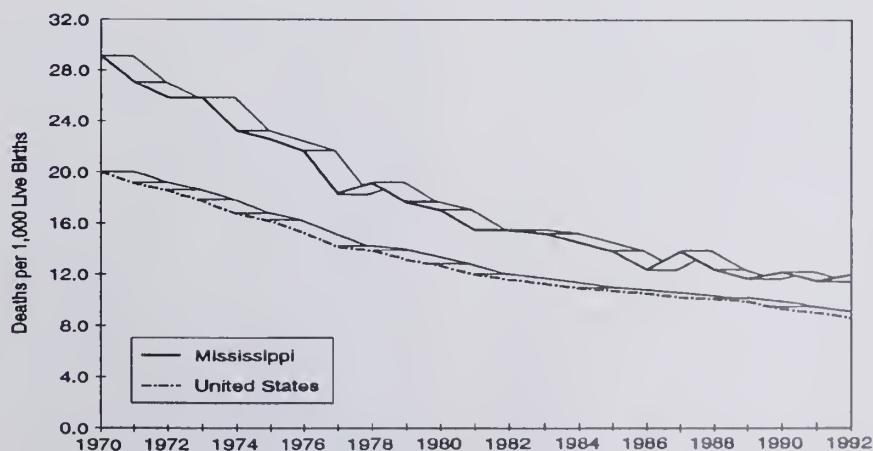
Since 1988, Mississippi's infant mortality rates have fluctuated between 12.3 and last year's all-time low of 11.4. For the past five years, the rates have see-sawed around a center-point of 11.86 deaths per 1,000 children under one-year-old. Mississippi's 1992 rate remains higher than the rates of neighboring states. All other Southeastern states have rates at or below 10.5.

"None of our statistical analysis or individual records review has identified the reasons Mississippi's rates have leveled off while the nation as a whole seems to maintain a steady decrease," Dr. Thompson said. Over the past 20 years, the state experienced a steady trend of decreasing infant mortality rates until figures began to level in 1988.

Combined data from the State Department of Health, Medicaid, welfare agencies, and private health care providers might help identify

(continued)

Infant Mortality Rates  
Mississippi and United States, 1970-1992



Note: U.S. rates for 1991 and 1992 are provisional

the state's options for maintaining a decreased infant mortality rate, Dr. Thompson said.

Sharing patient loads between private physicians and the state's county health departments is one option, said Hazel Gaines, RN, MS, director of MSDH Perinatal Services. "In the health departments, we are providing almost 56 percent of the state's prenatal care," Ms. Gaines said. Early prenatal care greatly reduces the chances of infant death and birth defects, she added.

Last year's overall infant mortality figure includes a rate of 7.8 for white babies, up from 7.4 in 1991, and a 16.1 rate among non-white infants, up from 15.5 the previous year. Across the nation, non-white infant mortality rates are generally twice as high as the rates among white infants, Ms. Gaines said.

"All kinds of studies have been done on the subject," Ms. Gaines said. "At one time, studies looked at poverty levels, education levels, and genetic conditions. No cause has been pinpointed, but we do know that the poor have higher rates." Also, both non-white and teenaged expectant mothers tend to seek prenatal care at a late date, Gaines added. In Mississippi, 74.6 percent of all expectant mothers get prenatal care before the first trimester of pregnancy passes.

#### **Infant Mortality**

In 1992, 508 children under the age of 1 died in Mississippi. A breakdown of the causes of death:

1. Birth abnormalities, 96
2. Sudden infant death syndrome, 83
3. Short gestation or low birthweight, 59
4. Respiratory distress syndrome, 28
5. Accidents, 24
6. Infections during perinatal period, 18
7. Maternal complications, 14
8. Oxygen deprivation or birth asphyxia, 11
9. Complications of placenta, cord, membranes, 9
10. Pneumonia and influenza, 7

\*\*\*

## **Governor Fordice OKs Measure to Focus Medicaid on Teen Mothers**

Jackson, MS — Gov. Kirk Fordice approved a measure that will relieve parents of many financial hardships connected with a pregnant teenager. The act will shift Medicaid eligibility to the teen's financial need. Previous eligibility was based on the family's income. Joyce Johnson, director of state Department of Human Service's Family and Children's Services division, made the announcement during a Governor's Infant Mortality Task Force meeting in Jackson.

The increased coverage would extend to about 1,450 teenagers, said Fordice spokesman John Arledge. The Medicaid extension goes into effect retroactively July 1 after approval by the federal Health Care Financing Administration. The state's initial outlay hasn't been determined but will result in long term savings. "Taking care of mothers in that age group will be more cost-effective than taking care of premature babies, which is a great possibility in dealing with teenage mothers," Arledge said.

\*\*\*



# The University of Mississippi Medical Center's Antenatal Diagnostic Unit: On The Cutting Edge of Tomorrow

**WILLIAM E. ROBERTS, MD**  
**KENNETH G. PERRY, JR., MD**  
**RICK W. MARTIN, MD**  
**JOHN C. MORRISON, MD**  
**JAMES N. MARTIN, JR., MD**

**A**ntenatal diagnosis has a colorful history that spans a brief period of just three decades. After techniques were developed in the early 1960s to allow tissue culture and growth of amniotic fluid cells with subsequent karyotyping, the amniotic space no longer was considered inaccessible. Initially, amniotic fluid was removed for study by blind insertion of a needle into the amniotic cavity. High resolution ultrasound now allows precise guidance of the needle into the amniotic cavity, the umbilical cord or even the fetus. Along with these advancements in the field of genetics and antenatal diagnosis have come the problems of maintaining an up-to-date awareness of current developments in association with technical expertise in this area of medicine. To meet this health care challenge in Mississippi, a comprehensive consultation and guidance service was needed.

The University of Mississippi Medical Center (UMMC) entered a new phase in this arena when it implemented a statewide protocol for maternal serum  $\alpha$ -feto-protein (MSAFP) screening in November 1985. In addition to providing the necessary laboratory assessment for MSAFP screening, UMMC and its Department of Obstetrics and Gynecology developed the expertise to offer consultation and targeted ultrasound scanning for the evaluation of MSAFP screen positive and screen-negative patients. From these beginnings, the Antenatal Diagnostic Service within the Ob-Gyn department's Division of Maternal-Fetal Medicine at UMMC expanded in both the number of patients seen as well as the demands for newer and more accurate methods of diagnosis. However, increased demand for services was constrained by facility limitations.

After the Antenatal Diagnos-

tic Service identified those areas of present and future need, UMMC was approached with plans to address these concerns. As a result of bipartisan cooperation and commitment to provide this valuable service for Mississippians, plans were initiated to create an Antenatal Diagnostic Unit (ADU). This project became a reality with the commencement of construction on August 12, 1992 and a projected opening of the ADU planned for January 1993.

### Physical Plan of the ADU

The ADU is located on either side of the 1-East wing of University Hospital and consists of over 2500 square feet devoted to antenatal diagnosis. Included within this dedicated facility are many areas including a separate scheduling and business office, two (2) fully equipped procedure rooms, one (1) fetal surgery room, a 3-bed antenatal fetal

evaluation area, and office space for support personnel.

A local area network system (LANS) for computers will be installed to support timely and efficient communication with providers and hospitals. Faxing capabilities will achieve nearly instantaneous transmission of ultrasound reports and consultation to physician offices and health departments throughout the state. Finally, database archiving will permit better documentation of the numbers of patients and procedures performed and the resultant outcomes and complications. We anticipate that this feature will enable us to provide more accurate, non-directive counseling pertaining to sensitivity and specificity of the tests and procedures which should help families to make better, more informed decisions.

New, state-of-the-art equipment is now available with a wide range of capabilities. These include doppler color flow mapping to fully evaluate the cardiovascular and peripheral vascular system of the fetus. M-mode cardiography allows precise documentation and diagnosis of fetal cardiac arrhythmias with the added capability to evaluate cardiac function. Pulsed doppler technique is utilized to measure placental and other fetal organ blood flow rates in order to detect early signs of organ dysfunction. Finally, endovaginal ultrasound, coupled with all of the previously mentioned capabilities of abdominal transducers, facilitates expansion of knowledge of the anatomy and organ function of the first trimester fetus. These advancements have already lead to the diagnosis of first trimester structural anomalies such as anencephaly and congenital heart defects. No doubt other structural and func-

tional abnormalities will be diagnosable in the future. This increase in knowledge and awareness of fetal conditions will impact upon prenatal care and may alter the time, method and location of delivery.

#### Function of the ADU

The primary function of the ADU is to provide prenatal diagnosis and consultation for physicians with patients at risk for a fetus with serious genetic disorders or malformations. A large multicenter study in the 1960s revealed that 6.5% of newborn infants have major or minor congenital abnormalities (Table I). Although these abnormalities represent numerous different and specific defects in genetic and embryologic development, the causes of human malformation can be stratified into four (4) distinct categories (Table II). Although some patients are easily identified as being at increased risk to deliver a child with a congenital anomaly (e.g., maternal

age of 35 years or more at time of birth), others are identified by genetic or obstetric history. It is recommended all patients be surveyed with some type of screening device at the time they present for prenatal care (Table III). Even though utilization of this schema will not permit identification of all patients at risk, it will often indicate areas of concern where further evaluation is warranted.

For patients at risk, professionals in the ADU will provide timely consultation for appropriate assessments and diagnostic procedures to aid in the exclusion or definition of fetal malformation and injury. In addition, many patients with negative genetic histories will nevertheless be found to be at increased perinatal risk through abnormal MSAFP screening or after the performance of an ultrasound examination. Personnel in the ADU will assess these patients, provide a comprehensive and competent evaluation for the various

**Table I Percentage of Children Born with Congenital Anomalies**

Any anomaly	6.5%*
Major	3.2%
Minor	3.6%
Syndrome	0.4%
Tumor	0.3%

\* The sum of the subcategories do not equal the total as some infants had both major and minor anomalies.

Adopted: Heinonen OP, Slone D, Shapiro S. Birth Defects and Drugs in Pregnancy. Littleton, MA: Publishing Science Group, 1977.

**Table II Causes of Human Malformation**

- |                          |                          |
|--------------------------|--------------------------|
| 1. Cytogenetic disorders | 3. Polygenetic disorders |
| 2. Mendelian disorders   | 4. Teratogenic disorders |



**Table III Genetic Questionnaire**

1. Is there anyone in your immediate (i.e., parents and siblings) or in the immediate family of this baby's father with a history of delivering a child with:
  - a. a birth defect
  - b. a stillborn
  - c. mental retardation
  - d. a genetic disease
2. Has anyone in the immediate family had an excessive number of miscarriages (3 or more)?
3. Were you taking any prescription medication or over the counter drugs during the first trimester of pregnancy?
4. How much alcohol do you consume in a week? How much do you smoke? What other medications have you used during the past 3 months (i.e., pain medications, antibiotics, cocaine/crack, diet pills, etc.)?

causes of human malformation, and recommend a subsequent course of pregnancy management.

#### Cytogenetic Disorders

The experience at UMMC parallels that of other centers in this country with the largest group of patients who seek prenatal diagnosis being those at risk to deliver a child with a

chromosomal abnormality (aneuploidy). The risk of aneuploidy in pregnancy is directly related to advancing maternal age. All presently available techniques to evaluate at-risk patients are listed in Table IV and are associated with a low risk of pregnancy loss. Because the risk of an untoward outcome from these invasive antenatal diagnostic procedures is approximately equiva-

lent to the likelihood of delivering an aneuploid infant at a maternal age of 35 years, this has been the accepted age to recommend to patients that they consider prenatal genetic evaluation.

In spite of their equal and highly predictive ability to diagnose chromosomal disorders, genetic diagnostic procedures differ in technique and the time during gestation when they are performed. CHORIONIC VILLUS SAMPLING (CVS) is generally performed at 10 to 12 weeks gestation with results forthcoming in 7 to 10 days. The CVS procedure can be performed either by the abdominal or vaginal route with sufficient material obtained for analysis in over 95% of patients. Since September 1990, over 75% of CVS procedures at UMMC have been performed vaginally and there has not been a culture failure and only one patient in whom sufficient material could not be obtained for evaluation. The loss rate after the procedure is comparable to the 1 in 250 procedure-related risk of conventional genetic amniocentesis.

Earlier concerns regarding the CVS procedure have either been resolved or proven unfounded. These include the problem of confined placental mosaicism which has recently been addressed to conclude that CVS results are as reliable as amniocentesis results.<sup>1</sup> The second area of concern is the recent report of limb reduction defects in selected patients that undergo CVS procedures. Because these defects were seen infrequently and only in patients who underwent the procedure at  $\leq 9$  weeks gestational age, the protocol at UMMC was modified in May 1991 to perform the procedure only in the interval from 10 to 12 weeks. Recent data from large

**Table IV Presently Available Techniques to Diagnose Chromosomal Abnormalities**

Procedure	Time of Performance
Chorionic villus Sampling	10 to 12 weeks
Early amniocentesis	12 to 14 weeks
Conventional amniocentesis	$\geq 15$ weeks
Percutaneous Umbilical Blood Sampling (PUBS)	$\geq 22$ weeks or oligohydramnios

international centers have revealed no increased incidence of limb defects associated with CVS.<sup>2,3</sup>

**EARLY AMNIOCENTESIS** (12 to 14 weeks gestation) is a technique that is being utilized increasingly as an alternative to conventional genetic amniocentesis and CVS. Until the mid-1980s, amniocenteses were performed blindly and there was a high failure rate to obtain amniotic fluid at gestations less than 16 weeks. Also, genetic laboratories required a large amount of amniotic fluid for an acceptable level of culture success and this could be obtained safely only from the 16th week onward. Due to advances in ultrasound technology, operator expertise and laboratory techniques, sufficient amounts of amniotic fluid can now be successfully obtained by ultrasound-directed puncture after the 11th week of gestation. Results are forthcoming in 10 to 14 days with a risk-related loss and test reliability comparable with conventional genetic amniocentesis at  $\geq 15$  weeks gestation.

Despite CVS and early amniocentesis, conventional genetic amniocentesis is still the gold standard and the preferred technique for many patients. Some at-risk patients are not identified until the second trimester of pregnancy. As with early amniocentesis, the procedure is performed under ultrasound guidance but in a  $\geq 15$  week gestation and results are available in 10 to 21 days. In addition to a fetal karyotype, amniotic fluid in both early and conventional amniocenteses is assayed for AFP as a screen for neural tube defects (NTDs) and related renal/pulmonary/integument abnormalities. Because the amniotic cavity is not entered during a CVS procedure, such a screen is

not possible and one must rely upon MSAFP screening.

On occasion, patients are identified late in pregnancy with fetal conditions that warrant a rapid karyotype. Also, patients may have a severe degree of oligohydramnios which renders amniocentesis impossible. In these patients, percutaneous umbilical blood sampling (PUBS) and growth of fetal lymphocytes provide a fetal karyotype analysis in only 3 to 5 days. Because the risk of fetal loss with PUBS is approximately twice that of the other procedures, it is undertaken only when other procedures are not possible or when a rapid diagnosis is essential for pregnancy management.

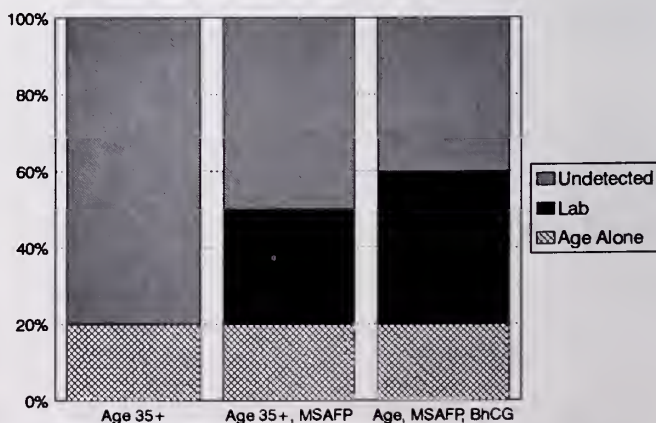
#### Biochemical Screening for Aneuploidy

Although increased MSAFP was initially promoted as a screening tool for NTDs, Merkatz and colleagues noted in 1984 that women carrying Down syndrome fetuses often had a lower than expected level of MSAFP.<sup>4</sup> Subsequent research in this area has revealed that, in addition to low MSAFP levels, women with

Down syndrome fetuses have higher than expected  $\beta$ HCG and lower than expected unconjugated maternal serum estriol ( $uE_3$ ) levels. These findings are of particular importance to women who, by age alone, would be considered at low risk for fetal aneuploidy. Only 20% of Down syndrome pregnancies are identified if maternal age alone is the screening criteria. However, the combination of low MSAFP and maternal age facilitates detection of 50% of Down syndrome pregnancies. Inclusion of  $\beta$ HCG determination with or without a maternal  $uE_3$  level raises the detection rate to 60% (Figure 1).

Because the cost of the  $\beta$ HCG determination with the MSAFP screen is very modest and achieves a false positive test result rate of only 5%, UMMC now routinely performs a  $\beta$ HCG determination with the MSAFP screen. Because the addition of estrogen testing to the screen appears not to be cost-effective, it is not performed routinely at UMMC. When MSAFP-age- $\beta$ HCG screening indicates that a mother's risk of fetal aneuploidy

**Figure 1 % Aneuploidy Detected by Different Screening Paradigms**



Adopted from: Evans MI et al, Reproductive Risks and Prenatal Diagnosis, 1992



exceeds the risk-related loss of a genetic amniocentesis (1 in 250), consideration for prenatal evaluation and diagnosis is recommended. However, regardless of the MSAFP and/or the  $\beta$ HCG value, the national standard of care is that a CVS or amniocentesis be recommended for consideration by all women who will be 35 years or older at the time of delivery.

### **Targeted Ultrasound Examination**

Ninety percent of fetuses with malformations occur in women without demonstrable risk factors. The use of prenatal ultrasound by competent examiners can detect many of these malformations. Indeed, for the detection of fetal malformations, a routine ultrasound at 18 to 20 weeks of gestation has a positive predictive value of 97% and a negative predictive value of 99%. When a fetal anomaly is detected during routine scanning, a targeted ultrasound examination is warranted to confirm the presence of the defect and to determine whether other potentially more severe abnormalities are also present. Because nearly one-third of fetuses with structural anomalies have chromosomal defects, consideration should be given for fetal karyotyping.<sup>5</sup> Furthermore, because one in four fetuses with sonographically diagnosed anomalies also have congenital heart defects, it is prudent under these circumstances to perform fetal echocardiography in conjunction with the targeted examination.<sup>6</sup> The yield of positive findings, if present, will be detected with greater frequency as the skill of the ultrasonographer increases.

To aid in better detection of Down syndrome fetuses in low risk patients, various biometric

measurements appear promising. These include nuchal skin fold thickness,<sup>7</sup> shortened femur length,<sup>8</sup> and pyelectasis at midgestation.<sup>9</sup> Although not recommended for patients already determined to be at risk for Down syndrome, obtaining such measurements seems prudent in low risk patients who undergo targeted scanning for other reasons.

### **Antenatal Fetal Evaluation and Therapy**

There is a 3-bed antenatal evaluation area in the ADU. The non-stress test (NST) and contraction stress test (CST) have proven value for the evaluation of fetal status. In addition to these fetal assessments, the ADU can perform fetal biophysical profiles (BPP), fetal acoustic stimulation (FAS) and doppler interrogation of the umbilical cord. These assessments provide additional insight in preterm gestations at risk for pregnancy-related complications.

An operating area in the ADU is available for highly specialized procedures involving multiple providers. These include PUBS (percutaneous umbilical blood sampling) procedures, stent placement for treatment of obstructive fetal uropathy and intrauterine intravenous fetal transfusion therapy.

### **Genetic Counselling**

At UMMC, there are certified genetic counselors and geneticists who have interest and expertise in molecular genetics, cytogenetics and biochemical genetics. The ADU relies heavily on the experienced and capable personnel within the Division of Genetics, Department of Preventive Medicine. Because the Genetics Group is located in the University Hospital, an unex-

pected need for a genetic evaluation is easily accomplished with minimum delay and inconvenience to patients.

### **Summary**

Prenatal diagnosis is a rapidly expanding field in the specialty of obstetrics. Modern providers of perinatal care must understand the fundamentals of inherited disease and keep abreast of advances in antenatal diagnosis. Pivotal in providing appropriate evaluation in this area is a referral center that is capable of affording the necessary evaluation, documentation and consultation. Although pregnancy termination is an option for some couples, many will use the information provided to prepare emotionally and financially for the birth of a child with special problems and needs. Some diagnoses will change obstetric management during the remainder of pregnancy or will lead to a recommendation for delivery at a tertiary medical facility. Other women with medical conditions warrant preconception counseling regarding pregnancy management and likelihood of a successful outcome. Patients with genetic disorders within their families may desire carrier detection through DNA analysis. Finally, women on medications at or near the time of conception frequently have concerns regarding potential teratogenesis. The ADU represents a commitment by both the Department of Obstetrics and Gynecology and the University of Mississippi Medical Center to furnish these services to providers and patients of the State of Mississippi.

The Directors of the Antenatal Diagnostic Unit are Dr. William E. Roberts and Dr. Kenneth G. Perry. Other specialists in the Division of Maternal-Fetal Medi-

cine include Dr. James N. Martin, Jr., Dr. John C. Morrison, Dr. Rick W. Martin, and physicians in the Maternal-Fetal Medicine Fellowship program. Another valuable member of the Antenatal Diagnostic Unit is Annette G. Walker who is the Coordinator for the UMMC MSAFP Program. To schedule procedures or obtain perinatal consultation, telephone the Antenatal Diagnostic Unit at (601) 984-4850 from 0800 to 1630 hours weekdays. □

2500 North State Street  
Jackson, MS 39216

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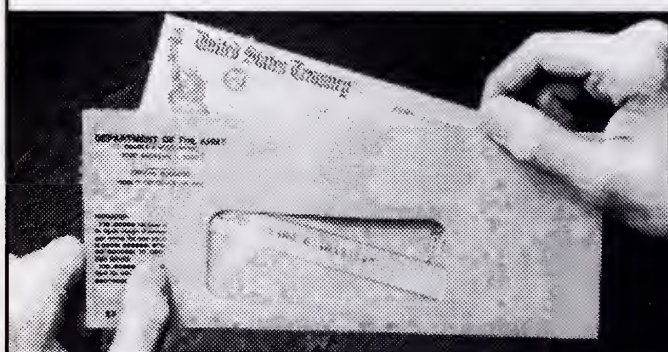
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*Dr. Roberts is Assistant Professor and Director of the Antenatal Diagnostic Unit, Dr. Perry is Assistant Professor, Dr. R. Martin is Associate Professor, Dr. Morrison is Vice-Chairman and Director of Research, Dr. J. Martin is Professor and Director of the Division of Maternal-Fetal Medicine, all from the Department of Obstetrics and Gynecology, at University of Mississippi Medical Center, Jackson, Mississippi*

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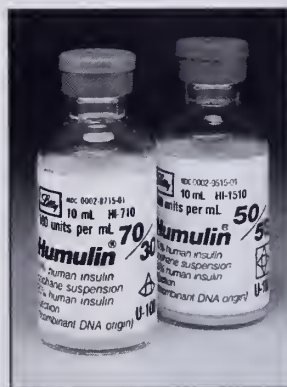





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# Women In Medicine

The American Medical Association declares September as *Women In Medicine* month. This special emphasis is a direct result of the recommendations contained in the 1980 report of the AMA's Ad Hoc Committee on Women Physicians. *Women in Medicine* month was established to bring attention to the growth and achievements of women physicians and medical students.

In 1990, the AMA established The AMA Women in Medicine Advisory Panel. This panel studies and advises the AMA Board of Trustees on issues and concerns of women within the Federation. Some of the panel's past and current projects include membership and leadership by

women physicians in the AMA; Gender Bias, Discrimination and Harassment; Health Access America; Women's Health; and flexible residency options. The Panel serves as a visible focus on the AMA's commitment to including and supporting women as active participants and leaders in organized medicine.

In recognition of *Women In Medicine* month, the *Journal MSMA* talked with Dr. Candace E. Keller, and Dr. Dwalia S. South regarding their thoughts on medicine. Both of these women are currently serving in leadership positions within the Mississippi State Medical Association.

.....



Candace E. Keller, MD, Hattiesburg, right.

◆ *What is your area of medical specialty and how long have you been in practice?*

Anesthesiology, in private practice since 1984.

◆ *Why did you choose medicine as your profession?*

I chose medicine as my profession because, from my childhood on, I've always had a desire to help people with illness get well and to help well people stay well. Medicine also allows me to pursue my interest in science.

◆ *Who has had the most influence on your career development and why?*

Dr. James Arens, who was the chairman of the



Anesthesiology Department at the University of Texas Medical Branch at Galveston. When I was a resident he strongly influenced my career through his excellent example as a physician, an anesthesiologist and as a leader in organized medicine.

♦ *What do you feel are some of the greatest challenges facing medicine today?*

Our greatest challenge will be maintaining our high standards of the practice of medicine, professionalism, and ethics in the changing environment in which we live and work. It will be important to remember and continue the aspects of medical practice which have been good and successful as we strive to further improve our healthcare system. Lastly, but most importantly, we must always put patients first.

♦ *Do you feel that these challenges are different or greater for women in medicine? Is so why?*

I believe women are ideally suited for the challenges facing medicine today. Women by nature are more adaptable to change, able to negotiate conflict, and willing to seek consensus. All of these qualities will benefit women in the coming era of medicine. In addition, the abilities to care and communicate will make women successful with their patients and communities.

While women have some unique barriers and needs, I do not believe our overall goals for the profession as a whole are any different.

♦ *Please make any additional comments about your profession.*

I have enjoyed and appreciated the opportunities I've had to participate in activities of the MSMA and AMA. It has been both educationally and personally enriching to work and fellowship with other colleagues from varying areas, practice settings and specialties. I encourage **All** physicians to become involved in both the State and National Organizations. The time is Now!

*Dr. Keller is currently serving as an MSMA Alternate Delegate to the AMA. She is also one of the ten members of the AMA Women in Medicine Advisory Panel.*

.....



**Dwalia S. South, MD, Ripley**

♦ *What is your area of medical specialty and how long have you been in practice?*

Family Practice, 12 years.

♦ *Why did you choose medicine as your profession?*

Recently I had a brief philosophical discussion with another doctor as to whether or not medicine was a "calling" for us as physicians. He said that the only "call" he ever got was the one the Dean of Admissions made to tell him he'd been accepted to medical school. We disagreed politely; I may not have defined it properly at the time. In one sense a calling can be any trade or occupation. But, I see medicine, especially Family Medicine, as somehow more than a job one simply selects to do. It is truly a "calling", a spiritual summons to a special service. There isn't a working day that passes that a family doctor doesn't encounter a dozen or so opportunities to minister to patients' spiritual as well as physical needs.

Some characteristics which I think are inherent to medicine as a career choice are a strong scientific bent, a boundless curiosity, an interest in the mechanics of human relationships as well as the human body, a genuine love for people of all kinds, and a desire to make lasting contributions to our community.

Being a doctor provides me the opportunity to make a good living in my hometown doing an important and interesting job.

My greatest enjoyment comes from daily opportunities to alleviate suffering. We all want to think that our time on earth has had a special meaning and that our lives have made a difference.

I've decided that, quite simply, I "need to be needed."

♦ *Who has had the most influence on your career development and why?*

Prior to medical school, I was influenced greatly by Dr. Jesse Mauney who was a pioneering female general practitioner in Tippah County. She practiced for 60 years until her death at age 92 and literally practiced medicine til the day she died, even treating patients from her sick bed.

I remember her treating me for asthma in the wee hours of the night many times as a child. Through her example I came to realize that medicine was a job that a woman could do and really do well. She was and still is highly revered in this little corner of the world.

After medical school I would have to say I was most influenced by the five men of the Ripley Medical Clinic with whom I practiced for seven years. They were Dr. Charlie Elliott, Dr. O. P. Stone, Dr. Tommy Simpson, Dr. Gerald Walden and Dr. T. L. Ketchum.

Currently, I'm in solo practice and I have come to love the freedom and independence that it brings, but I really miss the camaraderie we had back then. I learned a great deal more from those guys than I ever learned in school! This is why I believe preceptorships in Family Medicine are so very important to medical students.

In the last three years I've been most influenced by Dr. John Patterson of Pontotoc. He is a wonderful man who has sort of "taken me under his wing" and encouraged me into areas of leadership in the MSMA and MAFP. If more physicians throughout this country were like John Patterson, totally selfless and dedicated to the patient and the practice of medicine, I think the American medical climate might not be in its current predicament.

♦ *What do you feel are some of the greatest challenges facing medicine today?*

To me the greatest challenge is that arising from third party intervention into medicine.

I wish the practice of medicine could be once again somehow simply an interaction between the physician and the patient.

Physicians are smothered by paperwork, and patients now have an unrealistic expectation of health care and a diminishing respect for the medical profession as a whole.

Many people now view doctors as money-grub-

bing, country-clubbing, self-serving fat-cats. Somehow, we have to change this perception.

With our practice costs driven up the way they are, we do have to change a lot simply to meet our overhead. I don't understand it, and don't have any really great answers about how to remedy the problem. Health care today does cost too much; our system is getting monstrous.

But, I hate the notion of socialized medicine. Somewhere along the line people have to start assuming the responsibility for their health and the consequences of their behavior.

People have come to view the government as somehow accountable to their every need. Anything goes as long as someone else is picking up the tab.

I long for the old days I've heard about where a patient could simply come to me with their problem, be treated, pay me \$10.00 for their office visit and forget the blasted paper work. Think of the simplicity! (Think of the impossibility!)

Another great challenge we face is that our whole society is getting sick and dysfunctional. People laugh at you when you talk about Society's ills being brought on by "diminishing family values". But, it's more than a sound bite. Even in small-town Mississippi unwanted pregnancy, domestic violence, child abuse, alcohol and drug abuse, "life-style disease", and stress-related illness accounts for a large portion of my practice. How can we not "minister" to these people while we have them in our hands, even if it is only for 15-20 minutes? Sometimes our tasks as healers are truly overwhelming.

♦ *Do you feel that these challenges are different or greater for women in medicine? If so why?*

In the broadest sense, all doctors face the same challenges in meeting the needs of the people we serve in the very best way we can.

I think the best doctors (whatever their gender) function somehow androgenously, being an individual who brings to the profession of medicine, the best attributes of both sexes. A truly good physician (man or woman) will possess the masculine attributes of strength, stamina, and decisiveness and the feminine qualities of caring, communicating and nurturing.

From the standpoint of women physicians in the day-to-day world, yes, the challenges are a bit different. Especially if you choose to marry and have children. Not every woman physician does.



There is only so much you can get done vicariously and still have your kids recognize you as "my Momma." Thankfully, I have an excellent support system. My husband helps a lot, and so do my parents and other extended family who live nearby. (This is an added benefit of being in your hometown.)

We are (all of us) raising my children as best we know how. I think I am truly blessed in this respect.

It is easy for a woman doctor to fall in the trap of the "Superwoman Syndrome." I have a real tendency toward that, I have so much I want to ac-

complish. I used to spread myself too thin and try to be all things to all people. As I've grown older I've learned to become judiciously a bit more selfish with my time. For instance, I didn't run for County Coroner the last election because my husband said he'd leave me if I ever took that job again!

*Dr. South is currently serving as chairman of the MSMA Council On Medical Service and as a member of the MSMA Council On Public Information.*

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## Facts About Women In Medicine

### NUMBER OF WOMEN PHYSICIANS

- Women physicians will make up over 30 percent of the physician population by 2010.
- The largest group of women physicians is under the age of 44 (72%), whereas the largest number of male physicians is between the ages of 35 and 54 (50%).

### MEDICAL EDUCATION

- About 42 percent of the entering medical school class of 1992 was female. Of the total 15,554 students expected to graduate in 1993, 38 percent are women.
- In the past 20, years, the number of women applying to medical schools has surged from 6,000 in 1972-73 to 15,619 in 1992-93. During the same time, the total number of women enrolled in medical school rose from 6,099 to 25,933.

### SPECIALTY

- In 1992, and since 1980, most women have specialized in internal medicine with the largest single proportion in pediatrics (40 percent).

### WORK HOURS

- Female physicians work about 10 percent fewer hours a year than male physicians. They also work five to six less hours a week on practice activities.

### INCOME

- Female physicians earn 59 to 63 percent of what average male physicians earn. However, their income growth rate since 1981 has been higher. Female physicians are twice as likely to be employees rather than to be self-employed.
- Women physicians tend to have lower incomes because, among other factors, they work fewer hours, are over-represented in the lower-paying specialties, and are generally younger than male physicians.
- Income differences between female and male physicians are less per-visit than per-hour, indicating that female physicians may schedule fewer patients each hour.



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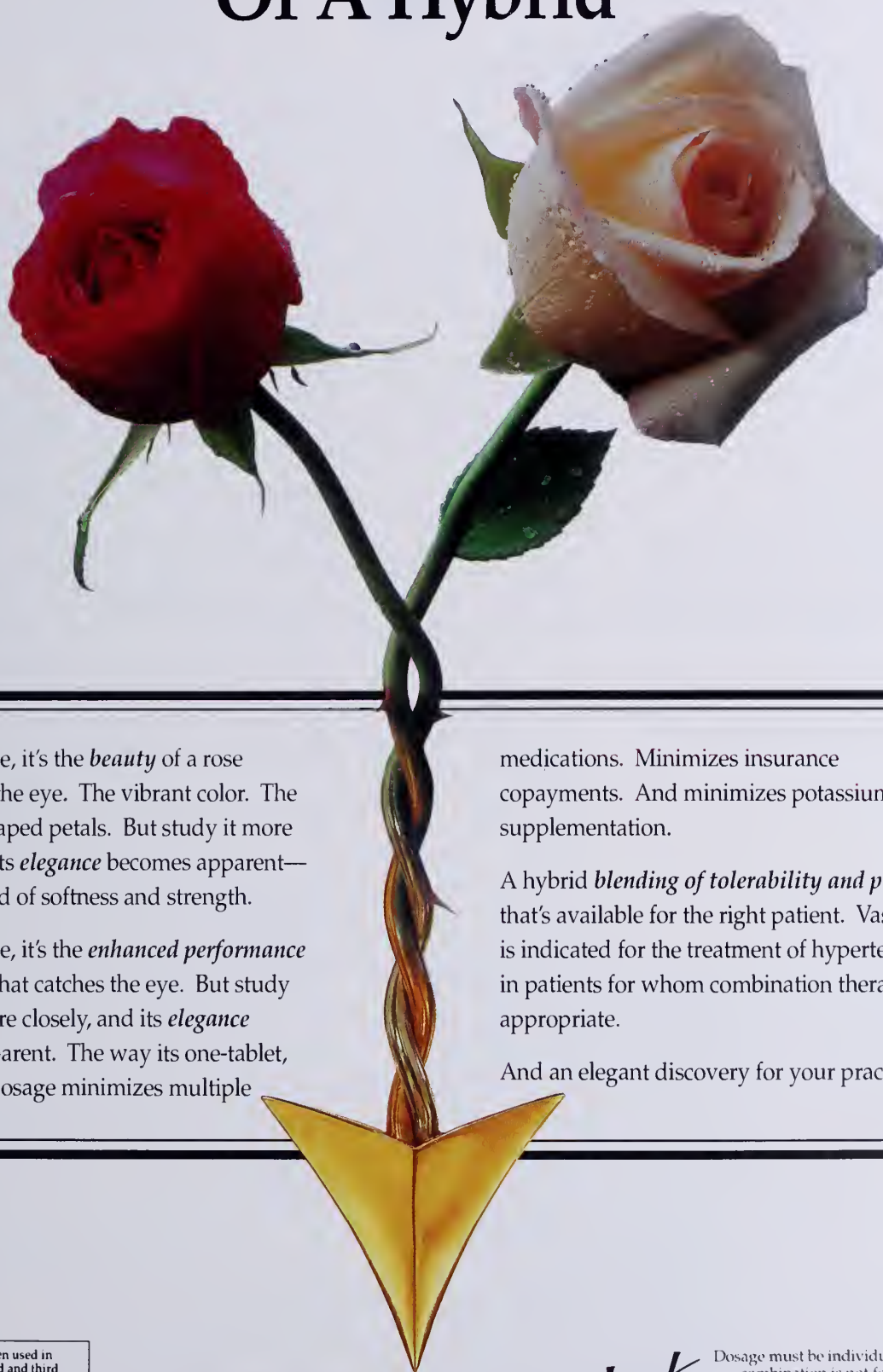
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# Discover The Elegance Of A Hybrid



At first glance, it's the *beauty* of a rose that catches the eye. The vibrant color. The delicately shaped petals. But study it more closely, and its *elegance* becomes apparent—a gentle blend of softness and strength.

At first glance, it's the *enhanced performance* of Vaseretic that catches the eye. But study Vaseretic more closely, and its *elegance* becomes apparent. The way its one-tablet, once-a-day dosage minimizes multiple

medications. Minimizes insurance copayments. And minimizes potassium supplementation.

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**USE IN PREGNANCY:** When used in pregnancy during the second and third trimesters, ACE inhibitors can cause injury and even death to the developing fetus. When pregnancy is detected, Vaseretic (Enalapril Maleate-Hydrochlorothiazide) should be discontinued as soon as possible. See WARNINGS, Fetal/Neonatal Morbidity and Mortality.

**VASERETIC® 10-25**  
Enalapril Maleate-Hydrochlorothiazide

*Next*

Dosage must be individualized; the fixed combination is not for initial therapy.

Evaluation of the hypertensive patient should always include assessment of renal function.

For a Brief Summary of Prescribing Information, see adjacent pages.



**TABLETS**  
**VASERETIC®**  
(ENALAPRIL MALEATE-HYDROCHLOROTHIAZIDE)

**USE IN PREGNANCY:** When used in pregnancy during the second and third trimesters, ACE inhibitors can cause injury and even death to the developing fetus. When pregnancy is detected, VASERETIC® (Enalapril Maleate-Hydrochlorothiazide) should be discontinued as soon as possible. See WARNINGS, Fetal/Neonatal Morbidity and Mortality.

**CONTRAINDICATIONS:** VASERETIC is contraindicated in patients who are hypersensitive to any component of this product and in patients with a history of angioedema related to previous treatment with an angiotensin converting enzyme inhibitor. Because of the hydrochlorothiazide component, this product is contraindicated in patients with anuria or hypersensitivity to other sulfonamide-derived drugs.

**WARNINGS:** General; Enalapril Maleate; Hypotension: Excessive hypotension was rarely seen in uncomplicated hypertensive patients but is a possible consequence of enalapril use in severely salt/volume depleted persons such as those treated vigorously with diuretics or patients on dialysis.

Syncope has been reported in 1.3 percent of patients receiving VASERETIC. In patients receiving enalapril alone, the incidence of syncope is 0.5 percent. The overall incidence of syncope may be reduced by proper titration of the individual components. (See PRECAUTIONS, Drug Interactions, and ADVERSE REACTIONS.)

In patients with severe congestive heart failure, with or without associated renal insufficiency, excessive hypotension has been observed and may be associated with oliguria and/or progressive azotemia, and rarely with acute renal failure and/or death. Because of the potential fall in blood pressure in these patients, therapy should be started under very close medical supervision. Such patients should be followed closely for the first two weeks of treatment and whenever the dose of enalapril and/or diuretic is increased. Similar considerations may apply to patients with ischemic heart or cerebrovascular disease, in whom an excessive fall in blood pressure could result in a myocardial infarction or cerebrovascular accident.

If hypotension occurs, the patient should be placed in the supine position and, if necessary, receive an intravenous infusion of normal saline. A transient hypotensive response is not a contraindication to further doses, which usually can be given without difficulty once the blood pressure has increased after volume expansion.

**Angioedema:** Angioedema of the face, extremities, lips, tongue, glottis and/or larynx has been reported in patients treated with angiotensin converting enzyme inhibitors, including enalapril. In such cases VASERETIC should be promptly discontinued and appropriate resuscitation and monitoring should be provided until complete and sustained resolution of signs and symptoms has occurred. In instances where swelling has been confined to the face and lips the condition has generally resolved without treatment, although antihistamines have been useful in relieving symptoms. Angioedema associated with laryngeal edema may be fatal. Where there is involvement of the tongue, glottis or larynx, likely to cause airway obstruction, appropriate therapy, e.g., subcutaneous epinephrine solution 1:1000 (0.3 mL to 0.5 mL) and/or measures necessary to ensure a patent airway, should be promptly provided. (See ADVERSE REACTIONS.)

Patients with a history of angioedema unrelated to ACE inhibitor therapy may be at increased risk of angioedema while receiving an ACE inhibitor (see also CONTRAINDICATIONS).

**Neutropenia/Agranulocytosis:** Another angiotensin converting enzyme inhibitor, captopril, has been shown to cause agranulocytosis and bone marrow depression, rarely in uncomplicated patients but more frequently in patients with renal impairment especially if they also have a collagen vascular disease. Available data from clinical trials of enalapril are insufficient to show that enalapril does not cause agranulocytosis at similar rates. Marketing experience has revealed several cases of neutropenia or agranulocytosis in which a causal relationship to enalapril cannot be excluded. Periodic monitoring of white blood cell counts in patients with collagen vascular disease and renal disease should be considered.

**Hydrochlorothiazide:** Thiazides should be used with caution in severe renal disease. In patients with renal disease, thiazides may precipitate azotemia. Cumulative effects of the drug may develop in patients with impaired renal function.

Thiazides should be used with caution in patients with impaired hepatic function or progressive liver disease, since minor alterations of fluid and electrolyte balance may precipitate hepatic coma.

Sensitivity reactions may occur in patients with or without a history of allergy or bronchial asthma.

The possibility of exacerbation or activation of systemic lupus erythematosus has been reported.

Lithium generally should not be given with thiazides (see PRECAUTIONS, Drug Interactions, Enalapril Maleate and Hydrochlorothiazide).

**Pregnancy, Enalapril-Hydrochlorothiazide:** There was no teratogenicity in rats given up to 90 mg/kg/day of enalapril (150 times the maximum human dose) in combination with 10 mg/kg/day of hydrochlorothiazide (2 1/2 times the maximum human dose) or in mice given up to 30 mg/kg/day of enalapril (50 times the maximum human dose) in combination with 10 mg/kg/day of hydrochlorothiazide (2 1/2 times the maximum human dose). At these doses, fetotoxicity expressed as a decrease in average fetal weight occurred in both species. No fetotoxicity occurred at lower doses; 30/10 mg/kg/day of enalapril-hydrochlorothiazide in rats and 10/10 mg/kg/day of enalapril-hydrochlorothiazide in mice.

When used in pregnancy during the second and third trimesters, ACE inhibitors can cause injury and even death to the developing fetus. When pregnancy is detected, VASERETIC should be discontinued as soon as possible. (See Enalapril Maleate, Fetal/Neonatal Morbidity and Mortality, below.)

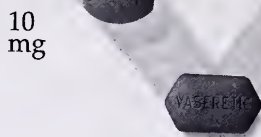
**Enalapril Maleate; Fetal/Neonatal Morbidity and Mortality:** ACE inhibitors can cause fetal and neonatal morbidity and death when administered to pregnant women. Several dozen cases have been reported in the world literature. When pregnancy is detected, ACE inhibitors should be discontinued as soon as possible.

The use of ACE inhibitors during the second and third trimesters of pregnancy has been associated with fetal and neonatal injury, including hypotension, neonatal skull hypoplasia, anuria, reversible or irreversible renal failure, and death. Oligohydramnios has also been reported, presumably resulting from decreased fetal renal function; oligohydramnios in this setting has been associated with fetal limb contractures, craniofacial deformation, and hypoplastic lung development. Prematurity, intrauterine growth retardation, and patent ductus arteriosus have also been reported, although it is not clear whether these occurrences were due to the ACE-inhibitor exposure.

These adverse effects do not appear to have resulted from intrauterine ACE-inhibitor exposure that has been limited to the first trimester. Mothers whose embryos and fetuses are exposed to ACE inhibitors only during the first trimester should be so informed. Nonetheless, when patients become pregnant, physicians should make every effort to discontinue the use of VASERETIC as soon as possible.

Rarely (probably less often than once in every thousand pregnancies), no

10  
mg



25  
mg

alternative to ACE inhibitors will be found. In these rare cases, the mothers should be apprised of the potential hazards to their fetuses, and serial ultrasound examinations should be performed to assess the intraamniotic environment.

If oligohydramnios is observed, VASERETIC should be discontinued unless it is considered lifesaving for the mother. Contraction stress testing (CST), a non-stress test (NST), or biophysical profiling (BPP) may be appropriate, depending upon the week of pregnancy. Patients and physicians should be aware, however, that oligohydramnios may not appear until after the fetus has sustained irreversible injury.

Infants with histories of *in utero* exposure to ACE inhibitors should be closely observed for hypotension, oliguria, and hyperkalemia. If oliguria occurs, attention should be directed toward support of blood pressure and renal perfusion. Exchange transfusion or dialysis may be required as means of reversing hypotension and/or substituting for disordered renal function. Enalapril, which crosses the placenta, has been removed from neonatal circulation by peritoneal dialysis with some clinical benefit, and theoretically may be removed by exchange transfusion, although there is no experience with the latter procedure.

No teratogenic effects of enalapril were seen in studies of pregnant rats, and rabbits. On a mg/kg basis, the doses used were up to 333 times (in rats), and 50 times (in rabbits) the maximum recommended human dose.

**Hydrochlorothiazide; Teratogenic Effects:** Reproduction studies in the rabbit, the mouse and the rat at doses up to 100 mg/kg/day (50 times the human dose) showed no evidence of external abnormalities of the fetus due to hydrochlorothiazide. Hydrochlorothiazide given in a two-liter study in rats at doses of 4-5.6 mg/kg/day (approximately 1-2 times the usual daily human dose) did not impair fertility or produce both abnormalities in the offspring. Thiazides cross the placental barrier and appear in cord blood.

**Neonatal Effects:** These may include fetal or neonatal jaundice, thrombocytopenia, and possibly other adverse reactions which have occurred in the adult.

**PRECAUTIONS:** General; Enalapril Maleate; Impaired Renal Function: As a consequence of inhibiting the renin-angiotensin-aldosterone system, changes in renal function may be anticipated in susceptible individuals. In patients with severe congestive heart failure whose renal function may depend on the activity of the renin-angiotensin-aldosterone system, treatment with angiotensin converting enzyme inhibitors, including enalapril, may be associated with oliguria and/or progressive azotemia and rarely with acute renal failure and/or death.

In clinical studies in hypertensive patients with unilateral or bilateral renal artery stenosis, increases in blood urea nitrogen and serum creatinine were observed in 20 percent of patients. These increases were almost always reversible upon discontinuation of enalapril and/or diuretic therapy. In such patients renal function should be monitored during the first few weeks of therapy.

Some patients with hypertension or heart failure with no apparent pre-existing renal vascular disease have developed increases in blood urea and serum creatinine, usually minor and transient, especially when enalapril has been given concomitantly with a diuretic. This is more likely to occur in patients with pre-existing renal impairment. Dosage reduction of enalapril and/or discontinuation of the diuretic may be required.

Evaluation of the hypertensive patient should always include assessment of renal function.

**Hemodialysis Patients:** Anaphylactoid reactions have been reported in patients dialyzed with high-flux membranes (e.g., AN 69) and treated concomitantly with an ACE inhibitor. In these patients consideration should be given to using a different type of dialysis membrane or a different class of antihypertensive agent.

**Hyperkalemia:** Elevated serum potassium (greater than 5.7 mEq/L) was observed in approximately one percent of hypertensive patients in clinical trials treated with enalapril alone. In most cases these were isolated values which resolved despite continued therapy, although hyperkalemia was a cause of discontinuation of therapy in 0.28 percent of hypertensive patients. Hyperkalemia was less frequent (approximately 0.1 percent) in patients treated with enalapril plus hydrochlorothiazide. Risk factors for the development of hyperkalemia include renal insufficiency, diabetes mellitus, and the concomitant use of potassium-sparing diuretics, potassium supplements and/or potassium-containing salt substitutes, which should be used cautiously, if at all, with enalapril. (See Drug Interactions.)

**Cough:** Cough has been reported with the use of ACE inhibitors. Characteristically, the cough is nonproductive, persistent and resolves after discontinuation of therapy. ACE inhibitor-induced cough should be considered as part of the differential diagnosis of cough.

**Surgery/Anesthesia:** In patients undergoing major surgery or during anesthesia with agents that produce hypotension, enalapril may block angiotensin II formation secondary to compensatory renin release. If hypotension occurs and is considered to be due to this mechanism, it can be corrected by volume expansion.

**Hydrochlorothiazide:** Periodic determination of serum electrolytes to detect possible electrolyte imbalance should be performed at appropriate intervals. All patients receiving thiazide therapy should be observed for clinical signs of fluid or electrolyte imbalance: hyponatremia, hypochloremic alkalosis, and hypokalemia. Serum and urine electrolyte determinations are particularly important when the patient is vomiting excessively or receiving parenteral fluids. Warning signs or symptoms of fluid and electrolyte imbalance, irrespective of cause, include dryness of mouth, thirst, weakness, lethargy, drowsiness, restlessness, confusion, seizures, muscle pains or cramps, muscular fatigue, hypotension, oliguria, tachycardia, and gastrointestinal disturbances such as nausea and vomiting.

Hyperkalemia may develop, especially with brisk diuresis, when severe cirrhosis is present, or after prolonged therapy. Interference with adequate oral electrolyte intake will also contribute to hypokalemia. Hypokalemia may cause cardiac arrhythmia and may also sensitize or exaggerate the response of the heart to the toxic effects of digitalis (e.g., increased ventricular irritability). Because enalapril reduces the production of aldosterone, concomitant therapy with enalapril attenuates the diuretic-induced potassium loss (see Drug Interactions, Agents Increasing Serum Potassium).

Although any chloride deficit is generally mild and usually does not require specific treatment except under extraordinary circumstances (as in liver disease or renal disease), chloride replacement may be required in the

treatment of metabolic alkalosis.

Dilutional hyponatremia may occur in edematous patients in hot weather; appropriate therapy is water restriction, rather than administration of salt except in rare instances when the hyponatremia is life-threatening. In actual salt depletion, appropriate replacement is the therapy of choice.

Hyperuricemia may occur or frank gout may be precipitated in certain patients receiving thiazide therapy.

In diabetic patients dosage adjustments of insulin or oral hypoglycemic agents may be required. Hyperglycemia may occur with thiazide diuretics. Thus latent diabetes mellitus may become manifest during thiazide therapy. The antihypertensive effects of the drug may be enhanced in the post-sympathectomy patient.

If progressive renal impairment becomes evident consider withholding or discontinuing diuretic therapy.

Thiazides have been shown to increase the urinary excretion of magnesium; this may result in hypomagnesemia.

Thiazides may decrease urinary calcium excretion. Thiazides may cause intermittent and slight elevation of serum calcium in the absence of known disorders of calcium metabolism. Marked hypercalcemia may be evidence of hidden hyperparathyroidism. Thiazides should be discontinued before carrying out tests for parathyroid function.

Increases in cholesterol and triglyceride levels may be associated with thiazide diuretic therapy.

**Information for Patients; Angioedema:** Angioedema, including laryngeal edema, may occur especially following the first dose of enalapril. Patients should be so advised and told to report immediately any signs or symptoms suggesting angioedema (swelling of the face, extremities, eyes, lips, tongue, difficulty in swallowing or breathing) and to take no more drug until they have consulted with the prescribing physician.

**Hypotension:** Patients should be cautioned to report lightheadedness especially during the first few days of therapy. If actual syncope occurs, the patients should be told to discontinue the drug until they have consulted with the prescribing physician.

All patients should be cautioned that excessive perspiration and dehydration may lead to an excessive fall in blood pressure because of reduction in fluid volume. Other causes of volume depletion such as vomiting or diarrhea may also lead to a fall in blood pressure; patients should be advised to consult with the physician.

**Hyperkalemia:** Patients should be told not to use salt substitutes containing potassium without consulting their physician.

**Neutropenia:** Patients should be told to report promptly any indication of infection (e.g., sore throat, fever) which may be a sign of neutropenia.

**Pregnancy:** Female patients of childbearing age should be told about the consequences of second- and third-trimester exposure to ACE inhibitors, and they should also be told that these consequences do not appear to have resulted from intrauterine ACE-inhibitor exposure that has been limited to the first trimester. These patients should be asked to report pregnancies to their physicians as soon as possible.

**NOTE:** As with many other drugs, certain advice to patients being treated with VASERETIC is warranted. This information is intended to aid in the safe and effective use of this medication. It is not a disclosure of all possible adverse or intended effects.

**Drug Interactions; Enalapril Maleate; Hypotension—Patients on Diuretic Therapy:** Patients on diuretics and especially those in whom diuretic therapy was recently instituted, may occasionally experience an excessive reduction of blood pressure after initiation of therapy with enalapril. The possibility of hypotensive effects with enalapril can be minimized by either discontinuing the diuretic or increasing the salt intake prior to initiation of treatment with enalapril. If it is necessary to continue the diuretic, provide medical supervision for at least two hours and until blood pressure has stabilized for at least an additional hour. (See WARNINGS.)

**Agents Causing Renin Release:** The antihypertensive effect of enalapril is augmented by antihypertensive agents that cause renin release (e.g., diuretics).

**Other Cardiovascular Agents:** Enalapril has been used concomitantly with beta adrenergic-blocking agents, methylglucosides, nitrates, calcium-blocking agents, hydralazine and prazosin without evidence of clinically significant adverse interactions.

**Agents Increasing Serum Potassium:** Enalapril attenuates diuretic-induced potassium loss. Potassium-sparing diuretics (e.g., spironolactone, triamterene, or amiloride), potassium supplements, or potassium-containing salt substitutes may lead to significant increases in serum potassium. Therefore, if concomitant use of these agents is indicated because of demonstrated hypokalemia they should be used with caution and with frequent monitoring of serum potassium.

**Lithium:** Lithium toxicity has been reported in patients receiving lithium concomitantly with drugs which cause elimination of sodium, including ACE inhibitors. A few cases of lithium toxicity have been reported in patients receiving concomitant enalapril and lithium and were reversible upon discontinuation of both drugs. It is recommended that serum lithium levels be monitored frequently if enalapril is administered concomitantly with lithium. **Hydrochlorothiazide:** When administered concurrently the following drugs may interact with thiazide diuretics:

**Alcohol, barbiturates, or narcotics—**potentiation of orthostatic hypotension may occur.

**Antidiabetic drugs (oral agents and insulin)—**dosage adjustment of the antidiabetic drug may be required.

**Other antihypertensive drugs—**additive effect or potentiation.

**Cholestyramine and colestipol resins—**Cholestyramine and colestipol resins bind the hydrochlorothiazide and reduce its absorption from the gastrointestinal tract by up to 85 and 43 percent, respectively. Thiazides may be administered two to four hours before the resin when the two drugs are used concomitantly.

**Corticosteroids, ACTH—**intensified electrolyte depletion, particularly hypokalemia.

**Pressor amines (e.g., norepinephrine)—**possible decreased response to pressor amines but not sufficient to preclude their use.

**Skeletal muscle relaxants, nondepolarizing (e.g., tubocurarine)—**possible increased responsiveness to the muscle relaxant.

**Lithium—**should not generally be given with diuretics. Diuretic agents reduce the renal clearance of lithium and add a high risk of lithium toxicity. Refer to the package insert for lithium preparations before use of such preparations with VASERETIC.

**Non-steroidal Anti-inflammatory Drugs—**In some patients, the administration of a non-steroidal anti-inflammatory agent can reduce the diuretic, natriuretic, and antihypertensive effects of loop, potassium-sparing and thiazide diuretics. Therefore, when VASERETIC and non-steroidal anti-inflammatory agents are used concomitantly, the patient should be observed closely to determine if the desired effect of the diuretic is obtained.

**Carcinogenesis, Mutagenesis, Impairment of Fertility:** Enalapril in combination with hydrochlorothiazide was not mutagenic in the Ames microbial mutagen test with or without metabolic activation. Enalapril-hydrochlorothiazide did not produce DNA single strand breaks in an *in vitro* alkaline elution assay in rat hepatocytes or chromosomal aberrations in an *in vitro* mouse

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marrow assay.

**Enalapril Maleate:** There was no evidence of a tumorigenic effect when enalapril was administered for 94 weeks to rats at doses up to 90 mg/kg/day (150 times the maximum daily human dose). Enalapril has been administered for 94 weeks to male and female mice at doses up to 90 and 180 mg/kg/day, respectively, (150 and 300 times the maximum daily dose for humans) and showed no evidence of carcinogenicity.

Neither enalapril maleate nor the active diacid was mutagenic in the Ames microbial mutagen test with or without metabolic activation. Enalapril was also negative in the following genotoxicity studies: sister chromatid exchange with cultured mammalian cells, the micronucleus test with mice, as well as in an *in vivo* cytogenetic study using mouse bone marrow. There were no adverse effects on reproductive performance in male and female rats treated with 10 mg/kg/day of enalapril.

**Hydrochlorothiazide:** Two-year feeding studies in mice and rats conducted under the auspices of the National Toxicology Program (NTP) uncovered no evidence of a carcinogenic potential of hydrochlorothiazide in female mice (at doses of up to approximately 600 mg/kg/day) or in male and female rats (at doses of up to approximately 100 mg/kg/day). The NTP, however, found equivocal evidence for hepatocarcinogenicity in male mice.

Hydrochlorothiazide was not genotoxic *in vitro* in the Ames mutagenicity assay of *Salmonella typhimurium* strains TA 98, TA 100, TA 1535, TA 1537, and TA 1538 and in the Chinese Hamster Ovary (CHO) test for chromosomal aberrations, or *in vivo* in assays using mouse germinal cell chromosomes, mouse hamster bone marrow chromosomes, and the *Drosophila* sex-linked recessive lethal trait gene. Positive test results were obtained only in the *in vitro* CHO Sister Chromatid Exchange (clastogenicity) in the Mouse Lymphoma Cell (mutagenicity) assays, using concentrations of hydrochlorothiazide of 1.43 to 1300 µg/mL, and in the *Aspergillus nidulans* non-disjunction assay at an unspecified concentration.

Hydrochlorothiazide had no adverse effects on the fertility of mice and rats of either sex in studies wherein these species were exposed, via their diet, to doses of up to 100 and 4 mg/kg, respectively, prior to conception and throughout gestation.

**Lactation:** Pregnancy Categories C (first trimester) and D (second and third trimesters). See WARNINGS, Precautions, Pregnancy Categories C, Fetal/Neonatal Morbidity and Mortality.

**Nursing Mothers:** Enalapril and enalaprilat are detected in human milk in trace amounts. Thiazides do appear in human milk. Because of the potential for serious reactions in nursing infants from either drug, a decision should be made whether to discontinue nursing or to discontinue VASERETIC taking into account the importance of the drug to the mother.

**Use in Children:** Safety and effectiveness in children have not been established.

**VERSE REACTIONS:** VASERETIC has been evaluated for safety in more than 1500 patients, including over 300 patients treated for one year or more. In clinical trials with VASERETIC, no adverse experiences peculiar to this combination drug have been observed. Adverse experiences that have occurred, have been limited to those that have been previously reported with enalapril or hydrochlorothiazide.

The most frequent clinical adverse experiences in controlled trials were: dizziness (8.6 percent), headache (5.5 percent), fatigue (3.9 percent) and cough (3.5 percent). Adverse experiences occurring in more than two percent of patients treated with VASERETIC in controlled clinical trials were: muscle cramps (2.7 percent), nausea (2.5 percent), asthenia (2.4 percent), orthostatic effects (2.3 percent), impotence (2.2 percent), and diarrhea (2.1 percent).

Clinical adverse experiences occurring in 0.5 to 2.0 percent of patients in controlled trials included: *Body As A Whole:* Syncope, chest pain, abdominal pain, *Cardiovascular:* Orthostatic hypotension, palpitation, tachycardia, *Digestive:* Vomiting, dyspepsia, constipation, flatulence, dry mouth, *Nervous/Psychiatric:* Anxiety, nervousness, paresthesia, somnolence, vertigo, *Skin:* Pruritus, rash, *Other:* Dyspnea, gout, back pain, arthralgia, diaphoresis, decreased libido, tinnitus, urinary tract infection.

**Angioedema:** Angioedema has been reported in patients receiving VASERETIC (0.6 percent). Angioedema associated with laryngeal edema may be fatal. If angioedema of the face, extremities, lips, tongue, glottis and/or larynx occurs, treatment with VASERETIC should be discontinued and appropriate therapy instituted immediately. (See WARNINGS.)

**Hypotension:** In clinical trials, adverse effects relating to hypotension occurred as follows: hypotension (1 percent), orthostatic hypotension (1.5 percent), other orthostatic effects (2.3 percent). In addition, syncope occurred in 1.3 percent of patients. (See WARNINGS.)

**Cough:** See PRECAUTIONS, Cough.

**Chemical Laboratory Test Findings, Serum Electrolytes:** See PRECAUTIONS.

**Creatinine, Blood Urea Nitrogen:** In controlled clinical trials, minor increases in blood urea nitrogen and urea creatinine, reversible upon discontinuation of therapy, were observed in about 0.6 percent of patients with essential hypertension treated with VASERETIC. More marked increases have been reported in other enalapril experience. Increases are more likely to occur in patients with renal artery stenosis. (See PRECAUTIONS.)

**Serum Uric Acid, Glucose, Magnesium, and Calcium:** See PRECAUTIONS.

**Hemoglobin and Hematocrit:** Small decreases in hemoglobin and hematocrit (mean decreases of approximately 0.3 g percent and 1.0 vol percent, respectively) occur frequently in hypertensive patients treated with VASERETIC but are rarely of clinical importance unless another cause of anemia coexists. In clinical trials, less than 0.1 percent of patients discontinued therapy due to anemia.

**Liver Function Tests:** Rarely, elevations of liver enzymes and/or serum bilirubin have occurred. Other adverse reactions that have been reported with the individual components are listed below and, within each category, are in order of decreasing severity.

**Enalapril Maleate:** Enalapril has been evaluated for safety in more than 10,000 patients. In clinical trials, adverse reactions which occurred with enalapril were also seen with VASERETIC. However, since enalapril has been marketed, the following adverse reactions have been reported: *Body As A Whole:* Nephrotoxic reactions (see PRECAUTIONS, Hemodialysis Patients); *Cardiovascular:* Cardiac arrest, myocardial infarction or cerebrovascular accident, possibly secondary to excessive hypotension in high risk patients (see WARNINGS, Hypotension); pulmonary embolism and infarction; pulmonary edema; rhythm disturbances including atrial tachycardia and bradycardia; atrial fibrillation; hypotension; angina pectoris; *Digestive:* Ileus, pancreatitis, hepatic failure, hepatitis (hepatocellular [proven on rechallenge] or cholestatic); *Hematologic:* Rare cases of neutropenia, thrombocytopenia and bone marrow depression, a few cases of hemolysis in patients with G-6-PD deficiency have been reported in which a causal relationship to enalapril cannot be excluded; *Nervous/Psychiatric:* Depression, confusion, ataxia, peripheral neuropathy (e.g., paresthesia, dysesthesia); *Orogenital:* Renal failure, oliguria, renal dysfunction (see PRECAUTIONS), flank pain, gynecomastia; *Respiratory:* Pulmonary infiltrates, bronchospasm, pneumonia, bronchitis, rhinorrhea, sore throat and arthralgia, asthma, upper respiratory infection, *Skin:* Exfoliative dermatitis, toxic epidermal necrolysis, Stevens-Johnson syndrome, herpes zoster, erythema multiforme, urticaria, alopecia, flushing, photosensitivity; *Special Senses:* Blurred vision, taste alteration, anosmia, conjunctivitis, dry eyes, tearing.

**Miscellaneous:** A symptom complex has been reported which may include a positive ANA, an elevated erythrocyte sedimentation rate, arthralgia/arthritis, myalgia, fever, serositis, vasculitis, leukocytosis, sinusitis, photosensitivity, rash and other dermatologic manifestations.

**Fetal/Neonatal Morbidity and Mortality:** See WARNINGS, Pregnancy, Enalapril Maleate: Fetal/Neonatal Morbidity and Mortality.

**Hydrochlorothiazide:** *Body as a Whole:* Weakness, *Digestive:* Pancreatitis, jaundice (intrahepatic cholestatic), *Endocrine:* sialadenitis, cramping, gastric irritation, anorexia, *Hematologic:* Aplastic anemia, agranulocytosis, leukopenia, hemolytic anemia, thrombocytopenia; *Hypersensitivity:* Purpura, photosensitivity, urticaria, necrotizing angitis (vasculitis and cutaneous vasculitis), fever, respiratory distress including pneumonitis and pulmonary edema, anaphylactic reactions, *Musculoskeletal:* Muscle spasm; *Nervous System/Psychiatric:* Restlessness, *Renal:* Renal failure, renal dysfunction, interstitial nephritis (see WARNINGS); *Skin:* Erythema multiforme including Stevens-Johnson syndrome, exfoliative dermatitis including toxic epidermal necrolysis, alopecia; *Special Senses:* Transient blurred vision, xanthopsia.

Based on patient weight of 50 kg.

For more detailed information, consult your DuPont Pharma Representative or see Prescribing Information.

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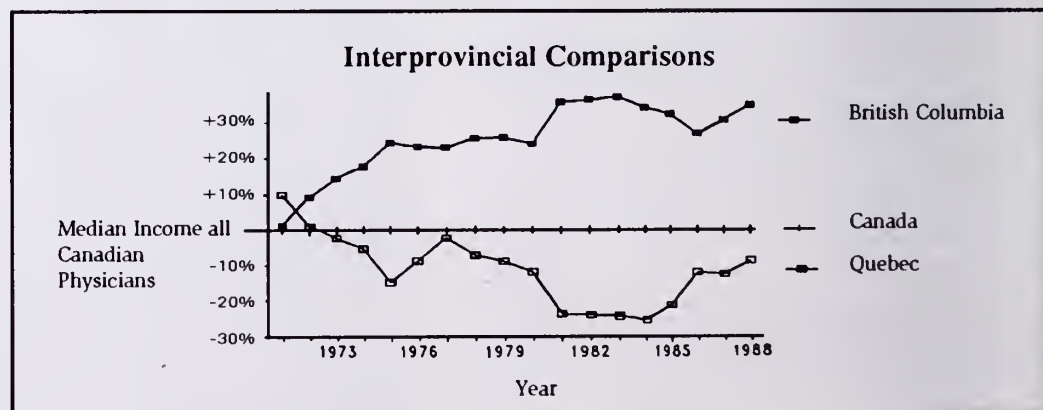


**The President's Page**  
DON Q. MITCHELL, MD

## United Voices

**A**t the Annual Session of the AMA a resolution was presented by the Washington Delegation which relates to my August article on unity. Their resolution, entitled "Divided We Fall", states that **"cost containment dominates discussions of health care issues"**. As a result, "potentially divisive professional fee schedules and other issues are being proposed with many radical changes already occurring. These forces and many others will tend to divide the House of Medicine."

This resolution, which was referred to the AMA Board of Trustees for decision, points out the critical need for the Federation of Medicine to be closely unified. The Canadian experience, which is depicted below graphically, was used as an example. It compares physician reimbursement in British Columbia where physicians speak with a united voice versus Quebec where they speak with a divided voice. As you can see, the difference is quite dramatic.



This reimbursement comparison is just further evidence that we need to be **united**. We need to speak with one voice. We need to support **our** MSMA with our time and talent. We need to get involved in **our** Physicians Care Network.

*(Continued on page 314)*



## Hippocrates Revisited

As health reform and rationing of health care become more likely, the physician is presented a painful dilemma: he or she is asked to weigh the interests of the patient against the interests of society as a whole. In attempting to resolve this conflict, refocusing on the Hippocratic oath seems appropriate because physicians have sworn to uphold that oath. Space constraints do not allow reprinting the entire Hippocratic oath here, but the following excerpt should serve to crystallize in our minds the proper position from a physicians perspective:

"I will follow that method of treatment which, according to my ability and judgement, I consider for the benefit of my patients, and abstain from whatever is deleterious and mischievous."

This statement clarifies the fact that, according to the oath of Hippocrates, the physician must serve his or her individual patients without consideration of society as a whole (except, by implication, where there is no conflict between the good of the patient and the good of society as a whole). It appears, therefore; that overt rationing of health care resources on a societal basis is in conflict with the

Hippocratic oath from the standpoint of the physician-patient relationship. The physician's duty is to advocate for the patient. Whatever constraints society chooses to impose on the availability of services may limit the choices available to patients based on physician recommendations, but the physician should not take such constraints into account when advising his or her individual patients regarding appropriate treatment options. That is, physicians should not act in complicity with socioeconomic rationing schemes when making professional recommendations to patients. Instead, "rationing" on an individual patient basis, within the bounds of medical ethics and with full patient/family participation, is the appropriate response for physicians, in my opinion.

Some might consider the Hippocratic oath archaic and suggest that it should not be taken literally, but it has served physicians and patients well for over 2000 years. As long as the oath we have sworn to uphold serves as the basis for the ethics of our profession, then we are well advised to remain steadfast in its defense.

**George E. Abraham, II, MD**  
Associate Editor

The editorial opinions expressed in this Journal are those of the indicated author. Editorial opinions are not expressions of the views, or official policies of The Mississippi State Medical Association. We encourage the membership to submit letters for publication regarding any opinion expressed or information contained in the Journal.

Because there are so many different proposed managed care organizations currently under discussion by physicians, hospitals and government, it is imperative that we understand the pros and cons of each type organization.

The key feature of our MS Physicians Care Network is that it is **physician-directed**. It is a network dedicated to preserving quality care and will be a well-managed group that can compete with hospitals and third-party payors on an equal footing. Our Physicians Care Network is **pro physician and patient**.

The MSMA sponsored Physicians Care Network steering committee will meet with managed care consultants for the project within 30 days and a membership packet for the Network will be mailed to all MSMA members shortly thereafter. Our MSMA will also offer an educational program about the Network to component societies and hospital medical staff meetings.

The opportunity is now — for above all, the MS Physicians Care Network provides us an organization that is dedicated to physician's empowerment in the interest of good patient care.

Your colleague,

*Don*

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**Action:** Yohimbine blocks presynaptic alpha-2 adrenergic receptors. Its action on peripheral blood vessels resembles that of reserpine, though it is weaker and of short duration. Yohimbine's peripheral autonomic nervous system effect is to increase parasympathetic (cholinergic) and decrease sympathetic (adrenergic) activity. It is to be noted that in male sexual performance, erection is linked to cholinergic activity and to alpha-2 adrenergic blockade which may theoretically result in increased penile inflow, decreased penile outflow or both.

Yohimbine exerts a stimulating action on the mood and may increase anxiety. Such actions have not been adequately studied or related to dosage, although they appear to require high doses of the drug. Yohimbine has a mild anti-diuretic action, probably via stimulation of hypothalamic centers and release of posterior pituitary hormone.

Reportedly, Yohimbine exerts no significant influence on cardiac stimulation and other effects mediated by B-adrenergic receptors, its effect on blood pressure, if any, would be to lower it; however no adequate studies are at hand to quantitate this effect in terms of Yohimbine dosage.

**Indications:** Yocon<sup>®</sup> is indicated as a sympatholytic and mydriatic. It may have activity as an aphrodisiac.

**Contraindications:** Renal diseases, and patient's sensitive to the drug. In view of the limited and inadequate information at hand, no precise tabulation can be offered of additional contraindications.

**Warning:** Generally, this drug is not proposed for use in females and certainly must not be used during pregnancy. Neither is this drug proposed for use in pediatric, geriatric or cardio-renal patients with gastric or duodenal ulcer history. Nor should it be used in conjunction with mood-modifying drugs such as antidepressants, or in psychiatric patients in general.

**Adverse Reactions:** Yohimbine readily penetrates the (CNS) and produces a complex pattern of responses in lower doses than required to produce peripheral a-adrenergic blockade. These include, anti-diuresis, a general picture of central excitation including elevation of blood pressure and heart rate, increased motor activity, irritability and tremor. Sweating, nausea and vomiting are common after parenteral administration of the drug.<sup>1,2</sup> Also dizziness, headache, skin flushing reported when used orally.<sup>1,3</sup>

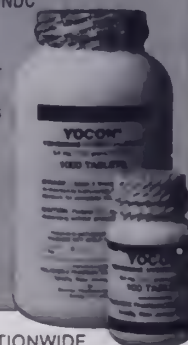
**Dosage and Administration:** Experimental dosage reported in treatment of erectile impotence.<sup>1,3,4</sup> 1 tablet (5.4 mg) 3 times a day, to adult males taken orally. Occasional side effects reported with this dosage are nausea, dizziness or nervousness. In the event of side effects dosage to be reduced to 1/2 tablet 3 times a day, followed by gradual increases to 1 tablet 3 times a day. Reported therapy not more than 10 weeks.<sup>3</sup>

**How Supplied:** Oral tablets of Yocon<sup>®</sup> 1/12 gr. 5.4 mg in bottles of 100's NDC 53159-001-01 and 1000's NDC 53159-001-10.

**References:**

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3. Weekly Urological Clinical letter, 27.2 July 4, 1983.
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## A Doctor's Adventures In Motherland

"Bark... Barrk..... Barrrrkk."  
 "Barkk... Barrrrkkk..... Barrookk."  
 "Barrkk..... Bark."

Maybe that was it. Maybe he won't cough anymore tonight. I told myself that if he coughed just one more time I would get up out of bed and go look for some cough syrup.

"Barrrk...."

Arrghh, that was the one. It was a February midnight and I had listened to assorted barks, whines, and groans all day in the clinic. I was keyed up and having a good deal of trouble relaxing. Fumbling around in the bathroom adjacent to Jack's bedroom I found a sample bottle of "Nite-Lite" children's cough syrup. It had always worked well before for his little tickling coughs and never interfered with his sleep.

"Here, little buddy, wake up and take a sip of this for Mom."

I know you're sitting there going... "a sip? .....a sip? This woman is a doctor and she's not using a measuring device??" I thought the same thing, but the spoons were a long, cold barefoot trek to the kitchen. At night, we sometimes measure by sips, swigs, or gulps out of those neat little sample bottles rather than counting cc's. Crude yes, imprecise yes, but usually rather effective.

Hopeful, I went back to my bed and tried to get warm again. After ten minutes or so, the sugary grapeness left him.

"Barrkk, bark..... whack, whack, whack" "Barrrrrook"

This continued for about thirty

minutes as I lay waiting for the stuff to go to work; it didn't.

Around 1:00 a.m. I reluctantly got up again and padded to the kitchen to inspect my makeshift sample closet for some stronger cough syrup. My eyes fell on some bright red bottles of "Tussi-Organidin" elixir. I grabbed a spoon and headed back.

"Okay, Jack-buddy, sit up and take some more medicine for Momma...."

Retrospectively, I guess the medicine was "for Momma" because Momma was the only person in the house apparently disturbed by the cough. Even Jack was sleeping through it.

Satisfied that I had done the right thing I went back to bed. Five minutes later another barking spasm was aborted by a loud liquid "urping" sound that I knew all too well. Jack has always been a master of throwing-up at the drop of a hat and tonight he blasted sheets, pillowcases and the bedside rug.

One to one-thirty was spent stripping his bed, shaking cherry-stained noodle fragments out of sheets in the back yard. (I swear I'll never feed that boy macaroni and cheese again... ever), and loading the washing machine.

All of this activity finally aroused Dad who got up to help haphazardly remake the bed while I changed Jack's clothes. Actually, I think I may have said something like "please get your butt up and help me!"

After we washed Jack's face, I

inspected him. He didn't seem to have any fever and was not audibly congested. Despite this, he was still coughing that non-productive gut-wrenching cough.

Dad, all-knowing and of the old "school of Dr. Mom" went to the kitchen, got a jar of honey and gave him two spoons of it. He then made Jack take a couple of sips of warm water, greased his chest with Vicks salve, and tucked him in. He never coughed again that night.

I lay there feeling humiliated and impotent for about an hour. I tried to console myself that the medicine I'd given him had finally kicked in. My husband in his utter smugness lost all of fifteen minutes of sleep.

Next morning Jack seemed fine, went to school and made the day without a hitch. That is, until midnight. I'd been asleep about an hour, having forgotten the previous night's episode. "Barrk.... Barrookk."

Okay, I was going to do things differently tonight. Let me see, I went straight to the kitchen and not to be outdone, I selected a good-tasting generic (is this a contradiction in terms?) cherry cough syrup with hydrocodone. I sneaked back, woke Jack, dosed him up and just for luck greased his chest with Vicks. Thirty minutes later he was still coughing loudly. Proudful, but no fool I got up and administered the "Sue Bee" and warm water. Once again, everything seem to click.

The next day at the clinic I picked up a bottle of "Phenergan with Codeine" elixir and that night he received a proper dose (prophylactically). We went through the

Vicks routine at his bedtime. By grabs, I was going to get at least one night's sleep that week!

He didn't cough at all that night.

I did this for two to three nights straight with excellent results. I.E. We all slept. (Jack, however, became addicted to Vicks salve and still can't go to sleep without it.) He never ran a fever and believe it or not I didn't slap him on an antibiotic as one is wont to do with a sick child. I reasoned that his cough was due to a post-nasal drip since it always seemed positional and nocturnal.

A few nights after I stopped premedicating him for bed, Jack woke up after sleeping only a couple of hours.

"Whine.....sniff.....snub....."  
"Whoooo.....sniff.....snub"  
"Oh, God what is it now? Son, are you having a bad dream?"

"I don't know, Momma.....snub, sniff..... I don't knooow.....I just can't sleep. I'm nervous."

"Nervous?"

Well, thinking it would fix everything I went to bed with him and hoped he would relax and go back to sleep. He didn't.

Sleep.....the prime directive.

Sleep.....The Final Frontier.

"Squirm, squirm..... snub, snub.....wiggle, kick" "Whine..... sniff.....snuffle."

This went on for the best part of an hour.

"What's the matter now, Babe?"

"I think I did have a bad dream, and I'm just nervous."

"Momma's here. It's alright. What did you dream about? Do you hurt anywhere?"

"Nooo-oooh, I'm just really nervous."

"Oh, crap. If we're not going to sleep anyway, we might as well get up. Maybe a movie will take both our minds off it."

We put "Wayne's World" in the

VCR. I brought Jack two "Children's Tylenol" and some Sprite to which he replied "Excellent.....party.....bonus!" We both laughed too loudly at Wayne and Garth, so loudly in fact that at about 2:00 a.m. Dad woke up and angrily demanded an explanation.

"I don't know what's wrong with him, he says he's nervous. I thought this might help relax him. He's stopped crying, but we're not getting any sleep this way."

Dr. Dad then located four orange "St. Joseph" baby aspirins, gave them to Jack, marched him to bed and we heard nary another whisper. By now I've learned to keep my mouth shut and accept defeat for what it's worth, (three glorious hours of sleep.)

Jack waked at 6:30 a.m. to finally announce his problem.

"Momma, my ear hurts!"

"A-HA! Supermom to the rescue!!"

I got out my otoscope and sure enough the boy had a fiery red left eardrum. It was at that moment that I realized that during the whole previous week I hadn't put a stethoscope to his chest, looked in his throat or actually taken his temperature. Suddenly, I felt like a really lousy doctor.

As I got the pink "Ceclor 250" samples out to the kitchen cabinet I tried to rationalize and put things in their proper perspective.

"Let's see your daddy cure this one with honey and Vicks Vaporub!!"

I prepared the medical armamentarium for his Granny to come over and stay with Jack while he missed kindergarten. I mixed up the "Ceclor", laid out the "Tylenol" and wrote out a schedule for her. When my mother came in the door the first thing she was "I told you this would happen if you let him ride his bicycle out in that cold wind without a cap!!!" Suddenly, I felt like a lousy mother, too.

As I drove to work I began feeling resentment for having to spend my whole day worrying with other folk's snotty-nosed, ill-behaved children while leaving my own ailing child at home for my mother to take care of.

"If President Clinton thinks there are a lot of kids in America receiving substandard medical care, he might look at physicians' children first. At mine anyway."

When I got to the office I tried to think about the mothers and children I would see that day who were not so lucky as me.....single mothers who didn't have a "Dr. Dad" at home to help them change dirty bedsheets at 2:00 a.m., who didn't have a trusted and all-knowing Granny who could stay home and nurse a sick little one while they went about business as usual, moms who have to miss a day's work to bring their child in to see me, and who then would leave without the forty bucks needed to buy that high-priced antibiotic I might prescribe.

Needless, to say Empathy was my middle name that day. I came home that evening to find a sassy and healthy five year old boy, humming while eating his "Batman" cereal in front of the T.V. with Granny at his side. His ears were full of sweet oil and cotton balls.

I sat there awhile and tried to decide if being a lousy mother sometime makes me a better doctor.....or is it the other way around? □

Dwalia South, MD  
Ripley, Mississippi

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## Mississippi Children's Immunization Awareness Project

The Mississippi Children's Immunization Awareness Project (MCIAP) was formed in November of 1991 as a collaborative force of private and public sector individuals and organizations dedicated to improving the immunization status of all Mississippi Children.

MCIAP is sponsored by the Mississippi Chapter of the American Academy of Pediatrics, the Mississippi Nurses Association and the Mississippi State Department of Health.

This project provided the framework which helped build and convene a statewide coalition committed to increasing the immunization levels of all Mississippi's two-year-olds.

The Mississippi Immunization Action Coalition was formed in 1992 with Mrs Pat Fordice, First Lady of Mississippi, serving as chairperson.

Since the Mississippi Children's Immunization Awareness Project was formed there have been significant increases in the number of two-year-olds in Mississippi who have achieved adequate immunizations. When the project began, 74% of the two-year-olds were immunized. By the end of 1992, 82%

of our two-year-olds were adequately immunized for DPT, OPV, and MMR. This figure is the second highest in the nation. Mississippians can be proud of this level of immunization in our two-year-old children. Our ultimate goal for the project in 1994 is to have 90% of all two year old's adequately immunized.

Numerous strategies have been implemented in the last two years for the MCIAP project which include:

1. Development and distribution of posters devised for immunization awareness through "Tear Drop" the clown. The "Tear Drop" character was created especially for MCIAP. This project was funded by grants from Connaught, Lederle and Merck, Sharp & Dohme.

2. Funding for a statewide immunization plan was obtained and the project has continued to assist in implementing the various aspects of the plan aimed at improving access to immunizations.

3. A Robert Wood Johnson Foundation Grant was secured to develop effective immunization tracking in the State.

4. The State participated in the 1993 Pre School Immuni-

zation Week on April 24-30. During the week public services messages were aired about the need for immunizations.

5. A chart has been developed of contraindications and precautions to immunizations and has been distributed to all child health care facilities in the State.

Additional projects that are in progress include:

- (1) The addition of TV commercials featuring "Tear Drop" the clown entitled "Tear Drop" talks about immunization awareness. These are public service spots, one with a nursery rhyme scenario and the other a rap scenario.

- (2) Paper tray liners printed with the immunization schedule were distributed by McDonald's restaurants.

- (3) The immunization schedule will also be printed on grocery sacks used to distribute WIC foods.

Numerous individuals have contributed to this project with Dr. Robert Abney serving as director. Plans are to proceed with the project so that Mississippi can continue to be at the top of the immunization statistics. □



## MSMA Board Holds Summer Meeting

MSMA's Board of Trustees and Officers held their summer meeting on August 7-8. They were joined by the Council of MSMA Past Presidents to hear a report on MSMA's managed care project and the Governor's Health Care Commission.

Among significant actions taken by the Board were:

- A steering committee was appointed to begin immediate implementation of an MSMA sponsored MS Physicians Care Network. The committee will meet with managed care consultants for the project within 30 days and a membership packet for the Network will be mailed to all MSMA members shortly thereafter. MSMA will also offer an educational program about the Network to component society and hospital medical staff meetings.
- MSMA will solicit each component society to send a representative to one of the following upcoming AMA meetings and pay one-half of his/her expenses: AMA Regional Medical Issue Meeting (Dallas, November 5 - see further information in this issue of *MSMA Report*); AMA House of Delegates Interim Meeting (New Orleans, December 5-8); AMA Leadership Conference (San Francisco, February 11-13). Complete details about these meetings will be furnished to each MSMA component society officer and will appear in future AMA and MSMA publications.
- MSMA will solicit each hospital medical staff in the state to send a representative to the AMA Hospital Medical Staff Section Meeting in New Orleans, December 2-4.
- The MSMA Alliance (formerly MSMA Auxiliary) will expand its Health Choice Program to three areas this association year (Hattiesburg, Jackson and Columbus), and will seek to encourage MSMA component societies as sponsors in their respective areas.
- MSMA will sponsor a "Medicine in Transition: Strategies for Change" workshop for members this fall which will deal with practice options, contractual considerations and how to thrive in a managed care environment.
- The MSMA House of Delegates will be called for a Special Session on January 18, 1994 in conjunction with the Annual Medical Socioeconomic Forum/Legislative Reception. The House will be asked to take action on various health care reform proposals expected to be introduced in the Mississippi Legislature, and will hear a status report on implementation of the MS Physicians Care Network. □

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## Governor's Commission on Health Care Holds Final Public Hearing In Jackson



The Governor's Commission on Health Care held its fourth and final public hearing during August. Three other public hearings were held previously around the state on July 1. These hearings provided opportunities for the public to express their concerns regarding health care in Mississippi.

The whole process began in May of this year when Governor Kirk Fordice named a 31-member commission headed by Vicksburg physician, Dr. Briggs Hopson. This group of legislators, medical, insurance and state agency professionals has until October 31 to send a report of their recommendations to the governor. Dr. Ellis Moffitt of Jackson and Dr. Ed Hill of Hollandale are representing the Mississippi State Medical Association on the Commission.

The commission's objective is to develop a strategy for addressing the financing, access and delivery of health care in Mississippi. After hearing much testimony during their regular Thursday meetings and the four public hearings, the commission has now divided into four groups. These groups will discuss both problems and solutions in the areas of financing, structure, tort reform and education.

Briggs Hopson, MD, of Vicksburg, at left, was appointed chairman of the Governor's Commission on Health Care by Governor Fordice in May of this year. Ellis Moffitt, MD of Jackson, right, is serving as one of MSMA's representatives on the Commission.

Other physicians serving on the Commission are Dr. J. Edward Hill, Hollandale, MSMA representative; Dr. Ed Thompson, State Health Officer; and Dr. Norman C. Nelson, Vice Chancellor for Medical Affairs, University of Mississippi Medical Center.



Dr. Susan Buttross, president of the MS Chapter of the American Academy of Pediatrics, presents information before the Governor's Commission on Health Care Reform during the public hearing held in Jackson.

Dr. Susan Buttross, president of the Mississippi Chapter of the American Academy of Pediatrics presented information about the health needs of Mississippi's children during the public hearing held in Jackson.

Dr. Gary D. Holdiness of Louisville also spoke at the Jackson hearing concerning the health needs of people in the rural areas of Mississippi. □

## **The 2nd Annual Mississippi State Coalition Against Domestic Violence Conference, *Family Violence And Sexual Assault: The Health Care Response* was held August 26-27 in Jackson.**

Approximately 100 people attended the second annual Mississippi State Coalition Against Domestic Violence Conference (MSCADV) held recently in Jackson at the Ramada Coliseum. Lark Johnson-Moss of Haven House Family Shelter, in Vicksburg serves as president of the MSCADV.

The conference entitled *Family Violence And Sexual Assault: The Health Care Response* was designed to provide the necessary information to all professionals so that they can: identify violence and sexual assault victims, understand their reactions to their victimization and to locate resources available in the community to help provide support and offer alternatives for change.

Dr. Diane Beebe, assistant professor, in the Department of Family Medicine, at the University of Mississippi Medical Center addressed one of the afternoon workshop session on the topic *Medical Perspectives in Dealing With Victims and Sexual Assault*.

Mary Krueger, PhD, Coordinator of Health Education and Adjunct Professor, Women's Health Studies/Public Health at Emory University in Atlanta served as the session keynote speaker. She spoke on the topics of *The Dynamics of Family Violence and Sexual Assault Within The Family*. Dr. Kruger has had a distinguished career as a health educator. She has served as the keynote speaker, workshop presenter or panelist at more than 38 conferences and symposiums and has produced approximately 14 publications.

Other speakers included: Debrynda Davey, EdD, RN, Associate Professor of Nursing, University of Mississippi Medical Center; Pat Flynn, JD, Assistant Attorney General, Mississippi Attorney Generals Office; Deborah Haller, BS, Senior Analyst, Serology Section, Mississippi Crime Laboratory; Lynn Glass-Heidenreich, RN; Jane Philo, RN, Executive Director, Gulf Coast Women's Center, Biloxi and James Baddley, Senior Vice President, Mississippi Hospital Association.

The Mississippi State Medical Association was a contributing supporter for this conference. □



Diane Beebe, MD, from the Department of Family Medicine at the University of Mississippi Medical Center was one of the conference speakers.

### **COMMENTS or QUERIES...**

The Editors of *Journal MSMA* invite you to comment on any material that appears in or is absent from the publication.

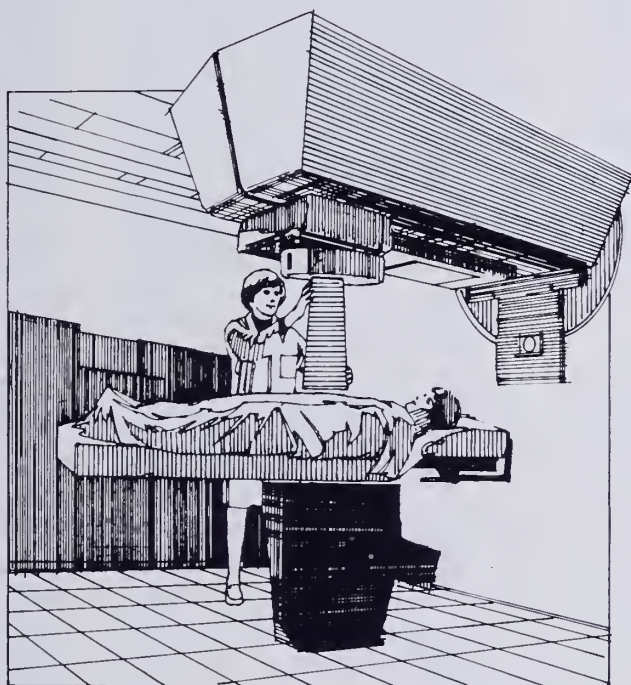
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# New Members

**Aleamar, Gilberto Orlando,** Jackson. Born Puerto Rico, July 4, 1961; MD, University of Puerto Rico School of Medicine, San Juan, Puerto Rico 1985; interned one year Mayaguez, Puerto Rico; general surgery residency, same, 1986 & 1987; otolaryngology residency, University Puerto Rico Hospitals, San Juan, Puerto Rico, 1987-89; otolaryngology residency, University Medical Center, Jackson, MS, 1989-91; elected by Central Medical Society.

**Barton, Jeffrey Scott,** Greenwood. Born Birmingham, AL, May 3, 1962; MD, University of Alabama School of Medicine, Birmingham, AL, 1988; interned and internal medicine residency, same, 1988-1991; gastroenterology fellowship, University of Arizona School of Medicine, Tucson, AZ, 1991-93; elected by Delta Medical Society.

**Bernardo Kerry L.,** Hattiesburg. Born San Mateo, CA, January 5, 1954; MD, University of California School of Medicine, San Francisco, CA, 1981; interned and neurosurgery residency, same, 1981-1984; fellowship in neurosurgery, same, 1984-86; elected by South Mississippi Medical Society.

**Bolton, Gary G.,** Jackson. Born Jackson, MS, September 20, 1985; MD, University of Mississippi School of Medicine, Jackson, MS, 1983; internal medicine residency, University Medical Center, Jackson, MS, 1983-86; dermatology residency Texas Tech University School of Medi-

cine, Lubbock, TX, 1990-93; elected by Central Medical Society.

**Booth, Patrick K.,** Hattiesburg. Born Memphis, TN, January 12, 1962; MD, University of Mississippi School of Medicine, Jackson, MS, 1987; general surgery residency, University of Tennessee Memorial Hospital, Knoxville, TN, 7/87-11/87; internal medicine residency, University Medical Center, Jackson, MS, 1/88-6/91; elected by South Mississippi Medical Society.

**Brawner, William C.,** Tupelo. Born Corinth, MS, June 20, 1962; MD, University of Mississippi School of Medicine, Jackson, MS, 1989; interned and ophthalmology residency, University Medical Center, Jackson, MS, 1989-93; elected by Northeast Medical Society.

**Campbell, Jonathan C., III,** Lucedale. Born Hinds Co., MS, March 2, 1964; MD, University of Mississippi School of Medicine, Jackson, MS, 1990; family practice residency, University of Alabama Medical Center, Tuscaloosa, AL, 1990-93; elected by South Mississippi Medical Society.

**Chain, Jeffrey R.,** Starkville. Born Pittsburgh, PA, April 2, 1957; MD, Jefferson Medical College of Thomas Jefferson University, Philadelphia, PA, 1983; interned LeHigh Valley Hospital Center, Allentown, PA, one year; orthopaedic surgery, Thomas Jefferson University, Philadelphia, PA, 1984-88;

elected by Prairie Medical Society.

**Cook, John W.,** Jackson. Born Memphis, TN, October 24, 1959; MD, University of Mississippi School of Medicine, Jackson, MS, 1989; interned and ob-gyn residency, same, 1989-93; elected by Central Medical Society.

**Dungan, V. Craig,** Meridian. Born Jersey Shore, PA, December 4, 1962; MD, University of Mississippi School of Medicine, Jackson, MS, 1990; interned and internal medicine residency Vanderbilt Hospital, Nashville, TN, 1990-93; elected by East Mississippi Medical Society.

**Fidei, Frank G.,** Houston. Born Pitts, PA, December 17, 1942; MD, Columbia University of Physicians and Surgeons, New York, NY, 1968; interned one year, Bronx Municipal Hospital, New York and 2 years surgery residency; surgery residency, 1971-73, Pensacola Educational Program, Pensacola, FL; elected by Northeast Mississippi Medical Society.

**Fontaine, David,** Born New Orleans, LA July 5, 1957; MD, Louisiana State University School of Medicine, New Orleans, LA 1987; pediatric residency, University of Texas Medical Branch, Galveston, TX, 1987-90; elected by Coast Counties Medical Society.

**Forks, Thomas P.,** Morton. Born Great Lakes, IL April 15, 1952; DO, University of Health



Sciences, College of Osteopathic Medicine, Kansas City, MO, 1988; interned one year Corpus Christi Osteopathic Hospital, Corpus Christi, TX; family practice residency, University Medical Center, Jackson, MS, 1989-91; elected by Central Medical Society.

**Jarmon, Henry M., Jr.,** Vicksburg. Born Vicksburg, MS, October 29, 1951; MD, University of Mississippi School of Medicine, Jackson, MS, 1978; general surgery and cardio-thoracic surgery residency, same, 1978-87; elected by West Mississippi School of Medicine.

**Lowe, Terry R.,** Hattiesburg. Born Hattiesburg, MS, January 1, 1965; MD, University of Mississippi School of Medicine, Jackson, MS, 1990; family practice residency, same, 1990-93;

elected by South Mississippi Medical Society.

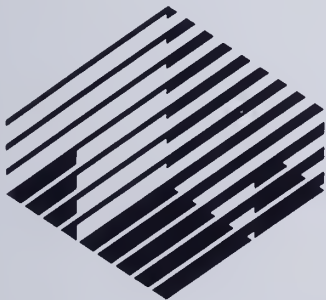
**Lundy, McKinley S.,** Jackson. Born Montgomery, AL, October 3, 1947; DO, Kansas City College of Osteopathic Medicine, Kansas City, MO, 1979; interned one year Center for Health Sciences of the Kansas City College of Osteopathic Medicine, Kansas City, MO; internal medicine residency University of Tennessee, Erlanger Medical Center, Chattanooga, TN, 1980-83; occupational medicine residency, Oklahoma College of Osteopathic Medicine and Surgery, Tulsa, OK, 1989-91; elected by Central Medical Society.

**Maddux, Robert F.,** Jackson. Born Batesville, MS, July 10, 1952; MD, University of Mississippi School of Medicine, Jackson, MS, 1983; psychiatry resi-

dency, University Medical Center, Jackson, MS, 1983-85; child psychiatry fellowship, same, 1/86-12/86 and 4/87-3/88; elected by Central Medical Society.

**Mills, Thomas P.,** Jackson. Born Elgin AFB, FL, March 7, 1960. MD, University of Mississippi School of Medicine, Jackson, MS 1987; interned and internal medicine residency, Vanderbilt University, Nashville, TN, 1987-90; fellowship Gastroenterology, University of Alabama at Birmingham, AL, 1990-93; elected by Central Medical Society.

**Partridge, R. Keith,** Wiggins. Born Natchez, MS, January 31, 1964; MD, University of Mississippi School of Medicine, Jackson, MS, 1990; interned and family practice residency, Jackson Madison County General Hospital, Jackson, TN, 1990-93;



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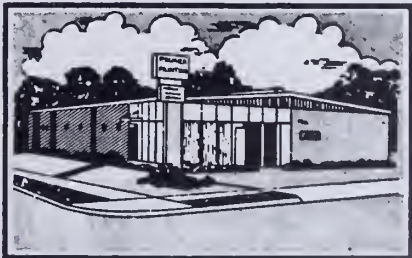
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elected by South Mississippi Medical Society.

**Powell, Rhonda H.**, Jackson. Born Birmingham, AL, September 8, 1961; MD, University of Alabama School of Medicine, Birmingham, AL, 1989; interned and ob-gyn residency, University Medical Center, Jackson, MS, 1989-93; elected by Central Medical Society.

**Searcy, Edwin E.**, Greenville. Born Nashville, TN, August 29, 1948; MD, University of Mississippi College of Medicine, Jackson, MS, 1973; interned and family practice residency, University Medical Center, Jackson, MS, 1973-76; elected by Delta Medical Society.

**Seicshnaydre, Michael A.**, Gulfport. Born Fort Huachuca, AZ, October 7, 1961; MD, Louisiana State University School of Medicine, New Orleans, LA, 1988; interned one year, Santa Barbara Cottage Hospital, Santa Barbara, CA; otolaryngology & head & neck surgery, Medical College of Virginia, Richmond, VA, 1989-93; elected by Coast Counties Medical Society.

**Sharp, Richard B.**, Tupelo. Born Colorado Springs, CO, February 28, 1962; MD, University of Arkansas School of Medicine, Little Rock, AR, 1989; physical medical & rehabilitation residency, University of Louisville School of Medicine & Frazier Rehab Center, Louisville, KY, 1989-93; elected by Northeast Mississippi Medical Society.

**Shields, Roderick A.**, Richland. Born Brandon, MS, February 27,

1962; MD, University of Mississippi School of Medicine, Jackson, MS, 1990; family practice residency, University Medical Center, Jackson, MS, 1990-93; elected by Central Medical Society.

**Thomae, Keith R.**, Brandon. Born Oshkosh, WI, September 21, 1960; MD, University of Wisconsin Medical School, Madison, WI, 1988; surgery residency, surgery residency, Loyola University Medical Center, Chicago, IL, 1988-93; elected by Central Medical Society.

**Tiwari, S. C.**, Jackson. Born Patna, December 2, 1959; MD, University of Mississippi College of Medicine, Jackson, MS, 1984; internal medicine residency, University of California, School of Medicine, Davis, CA, 1984-87; neurology residency, same, 1987-90; electrodiagnostic medicine fellowship, same, 1991-92; elected by Central Medical Society.

**Wallen, Reginald Mark**, Liberty. Born Hartford, CT, March 6, 1956; MD, University of Connecticut School of Medicine, Farmington, CT, 1985; interned and family practice residency Prince George Hospital Center, Cheverly, MD, 1985-88; elected by Amite-Wilkinson Counties Medical Society.

**Weber, Benjamin M.**, Laurel. Born Starkville, MS, March 12, 1962; MD, University of Mississippi School of Medicine, Jackson, MS, 1989; ob-gyn residency, University Medical Center, Jackson, MS, 1989-93; elected by South Mississippi Medical Society.

**Willis, Jeffrey Todd**, Collins. Born Shelby Co., TN, October

11, 1961; MD, University of Mississippi School of Medicine, Jackson, MS, 1989; interned and family practice residency, University Medical Center, Jackson, MS, 1989-90; elected by South Mississippi Medical Society.

**Woody, Walter W.**, Tupelo. Born Dayton, OH, April 8, 1953; MD, University of Mississippi School of Medicine, Jackson, MS, 1985; interned and internal medicine residency, University of Alabama Medical Center, Birmingham, AL, 1985-88; cardiology fellowship, University Medical Center, Jackson, MS, 1991-93; cardiology fellowship, University of Virginia Medical Center & Veterans Hospital, Salem & Charlottesville, VA, 1990-91; elected by Northeast Mississippi Medical Society.

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## Deaths

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**Bise, John R., III**, Jackson. Born New Orleans, LA, May 16, 1926; MD, Tulane University School of Medicine, New Orleans, LA, 1951; interned Charity Hospital, New Orleans, LA, 1951-52; ob-gyn residency, same, 1952-55; died August 6, 1993, age 67.

**Cook, Wendell H.**, Meridian. Born Neshoba County, MS, July 4, 1912; MD, Tulane University School of Medicine, New Orleans, LA, 1938; interned one year Southern Baptist Hospital, New Orleans, LA; died June 25, 1993, age 81.



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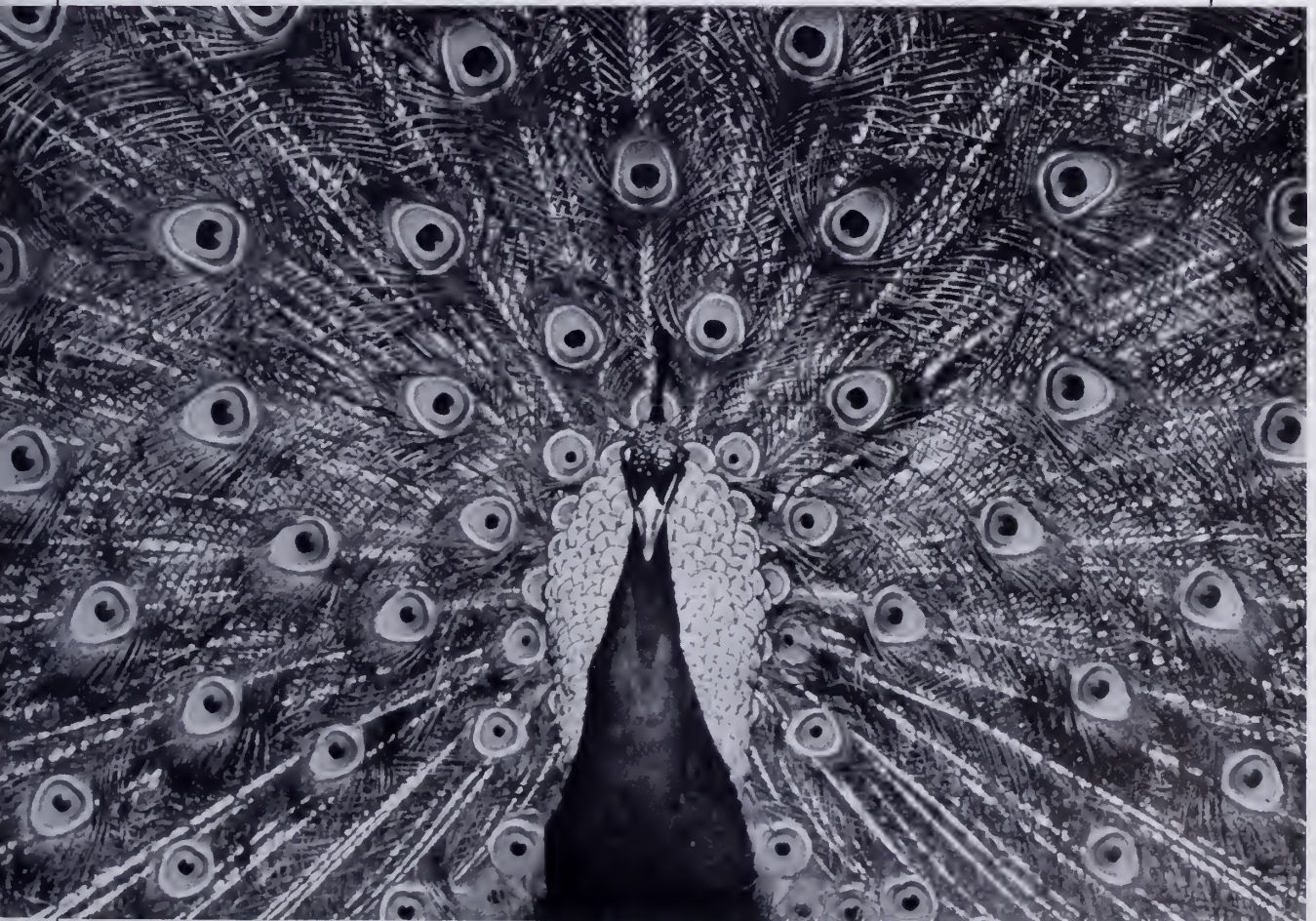
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**Joseph Robert Acosta** has associated with The Women's Clinic of Greenwood, P.A. for the practice of obstetrics and gynecology, 1604 Leflore Ave., Greenwood.

**Noah Archer** has associated with **John Coffey** and **Donald Killelea** in the practice of pediatrics, Children's Clinic, 136 Jefferson Davis Blvd., Natchez.

**Jeffery S. Barton** announces the opening of his office for the practice of gastroenterology, 1401 River Road, Greenwood.

**James L. Brown** of Tupelo announces his association with the Internal Medicine Associates of Tupelo, Ltd., and the relocation of his practice to 845 South Madison Street, Tupelo.

**William Ray Callender, Jr.**, has associated with **Joe Stanley Pulliam** of the Family Medical Center, for the practice of family medicine, 1467, Hwy. 1. South, Greenville.

**C. Ron Cannon**, of Jackson, recently served as program chairman of the May MS-LA O & O Society annual meeting held in Lafayette, Louisiana. He also served on the Long Range Planning Committee held in Washington, DC. in July.

**Lisa Leigh Chandler** has associated with **John P. Fullenwider** for the practice of pathology, 2301 South Lamar, Oxford.

**Curtis L. Collins** has associated with Sturgis, Henderson, and Proctor Pathology Laboratory, PA and Clinical Pathology Laboratory, Inc. in the practice of anatomic and clinical pathology, 1033 North Flowood Drive, Jackson.

**Robert Hugh Curry** and **Charles A. Ozborn** announce the opening of the Eupora Family Medical Clinic, 500 Highway 9 south, Eupora.

**David I. Dorrenbos**, a neurologist, has joined Rush Medical Group, P.A. of Meridian.

**V. Crag Dungan**, has associated with Rush Medical Group, P.A. of Meridian for the practice of internal medicine.

**Frank Fidei**, announces the opening of his office for the practice limited to General Surgery at Trace Regional Hospital, 1002 E. Madison, Houston, MS.

**John Robert Ford** a family physician in Vicksburg has been certified by the American Association of Medical Review Officers as a medical review officer.

**H. Lamar Gillespie** of Hattiesburg was recently named vice chairman of the Mississippi section of the American College of Obstetricians and Gynecologists.

**Fred Ingram** of Jackson is currently serving as chairman of the MS section of the American Col-

lege of Obstetricians and Gynecologists.

**Michael G. Kanosky** has associated with Plastic Surgery Associates for the practice of plastic and reconstructive surgery, hand surgery, cosmetic surgery, and head and neck surgery, 971 Lakeland Drive, Suite 515, Jackson, MS 39216.

**John C. Longest** of Starkville has been nominated for the prestigious Country Doctor of the Year Award, which is co-sponsored by the Country Doctor Museum in Bailey, N.C. and Staff Care, Inc., an interim physician staffing firm in Irving, Texas. Presented annually to one family practitioner in the United States, the Country Doctor of the Year Award recognizes the rural physician who best exemplifies the highest standards associated with the "old-fashioned" approach to the practice of medicine.

**Terry Lowe**, has associated with **Samuel Crosby**, **Wayne Hughes**, and **Michael May**, in the practice of Family Medicine at the Family Practice Clinic, 110 Millsaps Drive, Hattiesburg.

**F. Ellen McDaniel** has associated with Greenwood Radiology for the practice of Diagnostic Radiology, 1605 Strong Avenue, Greenwood.

**Jimmy D. Miller** announces the opening of his medical practice of neurosurgery, 812 Garfield St.,



uite A., Tupelo. He has also been elected to the Mississippi Foundation for Medical Care Board of Directors to serve through 1995.

**Frank J. Morgan, Jr.**, of Jackson, was re-elected for the third consecutive year, chairman of the Federation of State Medical Board's Examination Board (formerly FLEX Board) at the August meeting.

**Darden H. North**, of Jackson is currently serving as secretary-treasurer of the MS section of the American College of Obstetrics and Gynecologists.

**R. Keith Partridge** has associated with the Wiggins Clinic in

the practice of family medicine, 303 First Street, Wiggins.

**Stuart Todd Roth** has associated with **B. J. Jordan** and **C. M. Jordan** for the practice of radiology, 2301 South Lamar, Oxford.

**Buddy Savoie**, of Jackson recently made presentations and performed surgical demonstrations on *Traumatic Anterior Instability of the Shoulder*, *Arthroscopic Treatment of Multidirectional Instability* and *Arthroscopic Treatment of Fractures Dislocations of the Shoulder* at the Arthroscopic Surgery of the Shoulder, 10th Annual San Diego meeting. He also was an instructor for a meeting in Sydney

Australia of Combined Topics: *Overviews of Problems in the Shoulders, Knee and Spine* and presented lectures on *Total Shoulder Arthroplasty*, *Diagnosis and management of Instability of the Shoulder*, *Diagnosis and Management of Rotator Cuff Injuries*.

**Michael A. Selcshnaydre** has associated with **Donald L. Roberts**, for the practice of otolaryngology at the Center for Head and Neck Medicine & Surgery 4300 15th Street, Suite B, Gulfport.

**Nikhil Shah** has associated with The Greenville Clinic, P.A. for the practice of gastroenterology, 1705 Hospital Street, Greenville.

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**Richard B. Sharp** announces the opening of his medical practice of physical medicine and rehabilitation, 502 Eason Boulevard, Suite A, Tupelo.

**Clyde A. Sheehan**, announces the opening of his medical practice of child, adolescent and adult psychiatry, 808 Garfield Street, Suite A, Tupelo.

**Rod A. Shields** has associated with **James D. Polk**, Baptist/Richland Primary Care Center, for the practice of Family Medicine, 120 Scarbrough Drive, Richland.

**B. G. Spell** announced the relocation of his office to Arthritis

Surgery and Orthopaedic Institute, 631-B Lakeland East Drive, Jackson.

**Van D. Stone, III** has associated with North Mississippi Pediatrics, P.A. for the practice of pediatrics, 5 Medical Park Circle, Tupelo.

**Doyle Sumrall** has associated with **Michael Duckworth** for the practice of internal medicine, 515 Willowbrook Road, Columbus.

**Anthony L. Thomas**, a gastroenterologist, has associated with Internal Medicine Clinic, 1504 20th Avenue, Meridian.

**Sam C. Tumminello**, announces the new location of his dermatology practice to Physicians Plaza, Natchez Community Hospital, 151 Jefferson Davis Blvd., Suite E, Natchez.

**B. Michael Weber** has associated with the OB-GYN Group of Laurel, P.A. for the practice of obstetrics and gynecology, 1008 N. 15th Avenue, Laurel.

**Curtis D. Whittington, Jr.**, and **W. Granville Tabb, Jr.**, announce the association of **Toni J. Bertolet** and the formation of Mississippi Eyecare Associates. General ophthalmology and refractive surgery, suite 302, 1421 N. State Street, Jackson. □

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## STATE AND LOCAL

**Mississippi State Medical Association**, 126th Annual Session, May  
11-15, 1994, Jackson, Charles L. Mathews, Executive Director, 735  
Riverside Drive, PO Box 5229, Jackson 39296-5229.

**Mississippi Academy of Family Physicians**, Leontine Stevens, Execu-  
tive Secretary, PO Box 1215 Ridgeland 39158.

**Amite-Wilkinson Counties Medical Society**, 3rd Monday, March, June,  
September, December, James S. Poole, MD, Secy., The Gloster Clinic,  
PO Box D, Gloster 39638. Counties: Amite, Wilkinson.

**Central Medical Society**, 1st Tuesday, February, April, October, De-  
cember, 6:30 p.m., Primos Northgate Restaurant, Jackson. Patsy  
Douglas, Executive Secy., 735 Riverside Dr., Jackson 39202. Coun-  
ties: Hinds, Leake, Madison, Rankin, Scott, Simpson.

**Clarksdale and Six Counties Medical Society**, 3rd Wednesday, April,  
and 1st Wednesday, November, 2:00 p.m., Clarksdale, Glen L.  
Wegener, MD, Secy., PO Box 430, Clarksdale, MS 38614-0430.  
Counties: Coahoma, Quitman, Tallahatchie, Tunica.

**Coast Counties Medical Society**, January, March, June, and November.  
James E. Clarkson, MD, Secy., Mail: Ms. Leslie Johnson, PO Box  
128, Biloxi 39533. Counties: Hancock, Harrison.

**Delta Medical Society**, 2nd Wednesday, April and October. Walter H.  
Rose, MD, Secy., 122 E. Baker St., Indianola 38751. Counties: Boli-  
var, Humphreys, Leflore, Sunflower, Washington, Yazoo.

**East Mississippi Medical Society**, 1st Tuesday, February, April, June,  
October, December. Charles L. Wilkinson, MD, Secy., Mail: Ms.  
Jenkins, PO Box 4053, West Station, Meridian 39305. Counties:  
Clarke, Kemper, Lauderdale, Neshoba, Newton, Winston.

**Homochitto Valley Medical Society**. Meetings scheduled quarterly,  
David G. Hall, MD, Secy., 150 Jeff Davis Blvd, Suite 130, Natchez  
39120. Counties: Adams, Jefferson.

**North Central District Medical Society**, 3rd Wednesday, March, June,  
September, January, Gary Holdiness, MD, 332 Hwy 12 W, Kosciusko  
39090. Counties: Attala, Carroll, Choctaw, Granada, Holmes, Mon-  
tgomery, Webster.

**Northeast Mississippi Medical Society**, 1st Thursday, March, June,  
September, December. Richard L. Heyer, Jr., MD, Secy., Mail: Ms.  
Shirley Irwin, PO Box 3294, Tupelo 38803-3294. Counties: Alcorn,  
Calhoun, Chickasaw, Itawamba, Lee, Monroe, Pontotoc, Prentiss,  
Tishomingo, Union.

**North Mississippi Medical Society**, 1st Thursday, April, September, and  
3rd Thursday, January. Catherine E. Gleason, MD, Secy., 1306 Belk  
Blvd., Oxford 38655. Counties: Benton, Lafayette, Marshall, Panola,  
Tate, Tippah, Yalobusha.

**Prairie Medical Society**, 2nd Tuesday, March, June, September, De-  
cember, Joseph S. Bogges, MD, Secy., 515 Willowbrook Rd., Co-  
lumbus, MS 39701. Counties: Clay, Oktibbeha, Noxubee, Lowndes.

**Singing River Medical Society**, Quarterly, December, March, June and  
September. Hal Moore, MD, Secy., Mail: Ms. Beverly Small, 3003  
Shortcut Rd, Pascagoula 39567. County: Jackson.

**South Central Mississippi Medical Society**, 2nd Tuesday, March, June,  
September, December. Julian T. Janes, Jr., MD, Secy., PO Box 1910,  
McComb 39648. Counties: Copiah, Franklin, Lawrence, Lincoln,  
Pike, Walthall.

**South Mississippi Medical Society**, 2nd Thursday, March, June, Sep-  
tember, December. William A. Whitehead, MD, 415 South 28th  
Ave., Hattiesburg 39401-7246. Counties: Covington, Forrest, George,

Greene, Jasper, Jefferson Davis, Jones, Lamar, Marion, Perry, Smith,  
Wayne.

**West Mississippi Medical Society**, 2nd Tuesday, January, May, Sep-  
tember, November, 6:30 p.m. Maxwell's Restaurant, Vicksburg.  
Chester Masterson, MD, Secy., 1901 Mission 66, Vicksburg 39180.  
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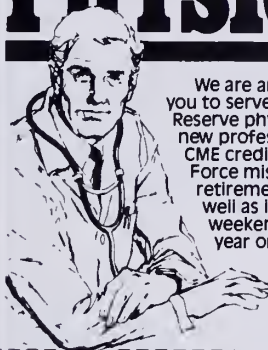
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## Index to Advertisers

**Bristol-Myers Squibb Company -**  
Pravachol ..... **third and fourth covers**

CancerPay Plus ..... 323  
CompHealth ..... 311

Disability Determination ..... 332  
Dupont Pharmaceuticals - Vaseretic  
Insert ..... 310 A-B, 311

Eli Lilly & Co. - Humulin ..... 305

Medical Assurance Co. of MS ..... 317  
Medley and Company ..... 314  
Mississippi Methodist Rehabilitation  
Center ..... **second cover**  
MS Emergency Association ..... 333  
MS Physicians Insurance Company ..... **4**  
MSMA Benefit Plan & Trust ..... 320

Palisades Pharmaceuticals - Yocon ..... 314  
Premier Printing ..... 325

The Doctors' Company ..... 327  
Trustmark ..... 325

US Air Force Reserve ..... 333  
US Army Active ..... 304  
US Army Reserve ..... 329



**Reference:** 1. Jones PH, et al. Once-daily pravastatin in patients with primary hypercholesterolemia: a dose-response study. *Clin Cardiol*. 1991;14:146-151.

**PRAVACHOL® (Pravastatin Sodium Tablets)**

**CONTRAINDICATIONS**

Hypersensitivity to any component of this medication.

Active liver disease or unexplained, persistent elevations in liver function tests (see WARNINGS).

Pregnancy and lactation. Atherosclerosis is a chronic process and discontinuation of lipid-lowering drugs during pregnancy should have little impact on the outcome of long-term therapy of primary hypercholesterolemia. Cholesterol and other products of cholesterol biosynthesis are essential components for fetal development (including synthesis of steroids and cell membranes). Since HMG-CoA reductase inhibitors decrease cholesterol synthesis and possibly the synthesis of other biologically active substances derived from cholesterol, they may cause fetal harm when administered to pregnant women. Therefore, HMG-CoA reductase inhibitors are contraindicated during pregnancy and in nursing mothers. **Pravastatin should be administered to women of childbearing age only when such patients are highly unlikely to conceive and have been informed of the potential hazards.** If the patient becomes pregnant while taking this class of drug, therapy should be discontinued and the patient apprised of the potential hazard to the fetus.

**WARNINGS**

**Liver Enzymes:** HMG-CoA reductase inhibitors, like some other lipid-lowering therapies, have been associated with biochemical abnormalities of liver function. Increases of serum transaminase (ALT, AST) values to more than 3 times the upper limit of normal occurring on 2 or more (not necessarily sequential) occasions have been reported in 1.3% of patients treated with pravastatin in the U.S. over an average period of 18 months. These abnormalities were not associated with cholestasis and did not appear to be related to treatment duration. In those patients in whom these abnormalities were believed to be related to pravastatin and who were discontinued from therapy, the transaminase levels usually fell slowly to pretreatment levels. These biochemical findings are usually asymptomatic although worldwide experience indicates that anorexia, weakness, and/or abdominal pain may also be present in rare patients.

As with other lipid-lowering agents, liver function tests should be performed during therapy with pravastatin. Serum aminotransferases, including ALT (SGPT), should be monitored before treatment begins, every six weeks for the first three months, every eight weeks during the remainder of the first year, and periodically thereafter (e.g., at about six-month intervals). Special attention should be given to patients who develop increased transaminase levels. Liver function tests should be repeated to confirm an elevation and subsequently monitored at more frequent intervals. If increases in AST and ALT equal or exceed three times the upper limit of normal and persist, then therapy should be discontinued. Persistence of significant aminotransferase elevations following discontinuation of therapy may warrant consideration of liver biopsy.

Active liver disease or unexplained transaminase elevations are contraindications to the use of pravastatin (see CONTRAINDICATIONS). Caution should be exercised when pravastatin is administered to patients with a history of liver disease or heavy alcohol ingestion (see CLINICAL PHARMACOLOGY: Pharmacokinetics/Metabolism). Such patients should be closely monitored, started at the lower end of the recommended dosing range, and titrated to the desired therapeutic effect.

**Skeletal Muscle:** Rhabdomyolysis with renal dysfunction secondary to myoglobinuria has been reported with pravastatin and other drugs in this class. Uncomplicated myalgia has also been reported in pravastatin-treated patients (see ADVERSE REACTIONS). Myopathy, defined as muscle aching or muscle weakness in conjunction with increases in creatine phosphokinase (CPK) values to greater than 10 times the upper limit of normal was reported to be possibly due to pravastatin in only one patient in clinical trials (<0.1%). Myopathy should be considered in any patient with diffuse myalgias, muscle tenderness or weakness, and/or marked elevation of CPK. Patients should be advised to report promptly unexplained muscle pain, tenderness or weakness, particularly if accompanied by malaise or fever. **Pravastatin therapy should be discontinued if markedly elevated CPK levels occur or myopathy is diagnosed or suspected. Pravastatin therapy should also be temporarily withheld in any patient experiencing an acute or serious condition predisposing to the development of renal failure secondary to rhabdomyolysis, e.g., sepsis; hypotension; major surgery; trauma; severe metabolic, endocrine, or electrolyte disorders; or uncontrolled epilepsy.**

The risk of myopathy during treatment with lovastatin is increased if therapy with either cyclosporine, gemfibrozil, erythromycin, or niacin is administered concurrently. There is no experience with the use of pravastatin together with cyclosporine. Myopathy has not been observed in clinical trials involving small numbers of patients who were treated with pravastatin together with niacin. One trial of limited size involving combined therapy with pravastatin and gemfibrozil showed a trend toward more frequent CPK elevations and patient withdrawals due to musculoskeletal symptoms in the group receiving combined treatment as compared with the groups receiving placebo, gemfibrozil, or pravastatin monotherapy. Myopathy was not reported in this trial (see PRECAUTIONS: Drug Interactions). One patient developed myopathy when clofibrate was added to a previously well tolerated regimen of pravastatin; the myopathy resolved when clofibrate therapy was stopped and pravastatin treatment continued. **The use of fibrates alone may occasionally be associated with myopathy. The combined use of pravastatin and fibrates should generally be avoided.**

**PRECAUTIONS**

**General:** Pravastatin may elevate creatine phosphokinase and transaminase levels (see ADVERSE REACTIONS). This should be considered in the differential diagnosis of chest pain in a patient on therapy with pravastatin.

**Hemolytic Anemia/Hypercholesterolemia:** Pravastatin has not been evaluated in patients with rare homozygous familial hypercholesterolemia. In this group of patients, it has been reported that HMG-CoA reductase inhibitors are less effective because the patients lack functional LDL receptors.

**Renal Insufficiency:** A single 20 mg oral dose of pravastatin was administered to 24 patients with varying degrees of renal impairment (as determined by creatinine clearance). No effect was observed on the pharmacokinetics of pravastatin or its 3 $\alpha$ -hydroxy isomeric metabolite (SO 31,906). A small increase was seen in mean AUC values and half-life (t<sub>1/2</sub>) for the inactive enzymatic ring hydroxylation metabolite (SO 31,945). Given this small sample size, the dosage administered, and the degree of individual variability, patients with renal impairment who are receiving pravastatin should be closely monitored.

**Information for Patients:** Patients should be advised to report promptly unexplained muscle pain, tenderness or weakness, particularly if accompanied by malaise or fever.

**Drug Interactions:** Immunosuppressive Drugs, Gemfibrozil, Niacin (Nicotinic Acid), Erythromycin: See WARNINGS: Skeletal Muscle.

**Antipyrine:** Clearance by the cytochrome P450 system was unaltered by concomitant administration of pravastatin. Since pravastatin does not appear to induce hepatic drug-metabolizing enzymes, it is not expected that any significant interaction of pravastatin with other drugs (e.g., phenytoin, quinidine) metabolized by the cytochrome P450 system will occur.

**Cholestyramine/Colestipol:** Concomitant administration resulted in an approximately 40 to 50% decrease in the mean AUC of pravastatin. However, when pravastatin was administered 1 hour before or 4 hours after cholestyramine or 1 hour before colestipol and a standard meal, there was no clinically significant decrease in bioavailability or therapeutic effect. (See DOSAGE AND ADMINISTRATION: Concomitant Therapy.)

**Warfarin:** In a study involving 10 healthy male subjects given pravastatin and warfarin concomitantly for 6 days, bioavailability parameters at steady state for pravastatin (parent compound) were not altered. Pravastatin did not alter the plasma protein-binding of warfarin. Concomitant dosing did increase the AUC and C<sub>max</sub> of warfarin but did not produce any changes in its anticoagulant action (i.e., no increase was seen in mean prothrombin time after 6 days of concomitant therapy). However, bleeding and extreme prolongation of prothrombin time has been reported with another drug in this class. Patients receiving warfarin-type anticoagulants should have their prothrombin times closely monitored when pravastatin is initiated or the dosage of pravastatin is changed.

**Cimetidine:** The AUC<sub>0-12hr</sub> for pravastatin when given with cimetidine was not significantly different from the AUC for pravastatin when given alone. A significant difference was observed between the AUC's for pravastatin when given with cimetidine compared to when administered with antacid.

**Digoxin:** In a crossover trial involving 18 healthy male subjects given pravastatin and digoxin concurrently for 9 days, the bioavailability parameters of digoxin were not affected. The AUC of pravastatin tended to increase, but the overall bioavailability of pravastatin plus its metabolites SO 31,906 and SO 31,945 was not altered.

**Gemfibrozil:** In a crossover study in 20 healthy male volunteers given concomitant single doses of pravastatin and gemfibrozil, there was a significant decrease in urinary excretion and protein binding of pravastatin. In addition, there was a significant increase in AUC, C<sub>max</sub>, and T<sub>max</sub> for the pravastatin metabolite SO 31,906. Combination therapy with pravastatin and gemfibrozil is generally not recommended.

In interaction studies with aspirin, antacids [1 hour prior to PRAVACHOL (pravastatin sodium)], cimetidine, nicotinic acid, or probucol, no statistically significant differences in bioavailability were seen when PRAVACHOL was administered.

**Other Drugs:** During clinical trials, no noticeable drug interactions were reported when PRAVACHOL was added to diuretics, antihypertensives, digoxin, converting-enzyme inhibitors, calcium channel blockers, beta-blockers, or nitroglycerin.

**Endocrine Function:** HMG-CoA reductase inhibitors interfere with cholesterol synthesis and lower circulating cholesterol levels and, as such, might theoretically blunt adrenal or gonadal steroid hormone production. Results of clinical trials with pravastatin in males and post-menopausal females were inconsistent with regard to possible effects of the drug on basal steroid hormone levels. In a study of 21 males, the mean testosterone response to human chorionic gonadotropin was significantly reduced (p<0.004) after 16 weeks of treatment with 40 mg of pravastatin. However, the percentage of patients showing a  $\geq$ 50% rise in plasma testosterone after human chorionic gonadotropin stimulation did not change significantly after therapy in these patients. The effects of HMG-CoA reductase inhibitors on spermatogenesis and fertility have not been studied in adequate numbers of patients. The effects, if any, of pravastatin on the pituitary-gonadal axis in pre-menopausal females are unknown. Patients treated with pravastatin who display clinical evidence of endocrine dysfunction should be evaluated appropriately. Caution should also be exercised if an HMG-CoA reductase inhibitor or other agent used to lower cholesterol levels is administered to patients also receiving other drugs (e.g., ketoconazole, spironolactone, cimetidine) that may diminish the levels or activity of steroid hormones.

**CNS Toxicity:** CNS vascular lesions, characterized by perivascular hemorrhage and edema and mononuclear cell

infiltration of perivascular spaces, were seen in dogs treated with pravastatin at a dose of 25 mg/kg/day, a dose that produced a plasma drug level about 50 times higher than the mean drug level in humans taking 40 mg/day. Similar CNS vascular lesions have been observed with several other drugs in this class.

A chemically similar drug in this class produced optic nerve degeneration (Wallenian degeneration of retinogeniculate fibers) in clinically normal dogs in a dose-dependent fashion starting at 60 mg/kg/day, a dose that produced mean plasma drug levels about 30 times higher than the mean drug level in humans taking the highest recommended dose (as measured by total enzyme inhibitory activity). This same drug also produced vestibulocochlear Wallenian-like degeneration and retinal ganglion cell chromatolysis in dogs treated for 14 weeks at 180 mg/kg/day, a dose which resulted in a mean plasma drug level similar to that seen with the 60 mg/kg dose.

**Carcinogenesis, Mutagenesis, Impairment of Fertility:** In a 2-year study in rats fed pravastatin at doses of 10, 30, or 100 mg/kg body weight, there was an increased incidence of hepatocellular carcinomas in males at the highest dose (p<0.01). Although rats were given up to 125 times the human dose (HD) on a mg/kg body weight basis, their serum drug levels were only 6 to 10 times higher than those measured in humans given 40 mg pravastatin as measured by AUC.

The oral administration of 10, 30, or 100 mg/kg (producing plasma drug levels approximately 0.5 to 5.0 times human drug levels at 40 mg) of pravastatin to mice for 22 months resulted in a statistically significant increase in the incidence of malignant lymphomas in treated females when all treatment groups were pooled and compared to controls (p<0.05). The incidence was not dose-related and male mice were not affected.

A chemically similar drug in this class was administered to mice for 72 weeks at 25, 100, and 400 mg/kg body weight, which resulted in mean serum drug levels approximately 3, 15, and 33 times higher than the mean human serum drug concentration (as total inhibitory activity) after a 40 mg oral dose. Liver carcinomas were significantly increased in high-dose females and mid- and high-dose males, with a maximum incidence of 90 percent in males. The incidence of adenomas of the liver was significantly increased in mid- and high-dose females. Drug treatment also significantly increased the incidence of lung adenomas in mid- and high-dose males and females. Adenomas of the eye Harderian gland (a gland of the eye of rodents) were significantly higher in high-dose mice than in controls.

No evidence of mutagenicity was observed *in vitro*, with or without rat-liver metabolic activation, in the following studies: microbial mutagen tests, using mutant strains of *Salmonella typhimurium* or *Escherichia coli*, a forward mutation assay in L5178Y TK +/– mouse lymphoma cells, a chromosomal aberration test in hamster cells, and a gene conversion assay using *Saccharomyces cerevisiae*. In addition, there was no evidence of mutagenicity in either a dominant lethal test in mice or a micronucleus test in mice.

In a study in rats, with daily doses up to 500 mg/kg, pravastatin did not produce any adverse effects on fertility or general reproductive performance. However, in a study with another HMG-CoA reductase inhibitor, there was decreased fertility in male rats treated for 34 weeks at 25 mg/kg body weight, although this effect was not observed in a subsequent fertility study when this same dose was administered for 11 weeks (the entire cycle of spermatogenesis, including epididymal maturation). In rats treated with this same reductase inhibitor at 180 mg/kg/day, seminiferous tubule degeneration (necrosis and loss of spermatogenic epithelium) was observed. Although not seen with pravastatin, two similar drugs in this class caused drug-related testicular atrophy, decreased spermatogenesis, spermatocytic degeneration, and giant cell formation in dogs. The clinical significance of these findings is unclear.

**Pregnancy: Pregnancy Category X:** See CONTRAINDICATIONS.

Safety in pregnant women has not been established. Pravastatin was not teratogenic in rats at doses up to 1000 mg/kg/day or in rabbits at doses of up to 50 mg/kg/day. These doses resulted in 20x (rabbit) or 240x (rat) the human exposure based on surface area (mg/meter<sup>2</sup>). However, in studies with another HMG-CoA reductase inhibitor, skeletal malformations were observed in rats and mice. PRAVACHOL (pravastatin sodium) should be administered to women of child-bearing potential only when such patients are highly unlikely to conceive and have been informed of the potential hazards. If the woman becomes pregnant while taking PRAVACHOL, it should be discontinued and the patient advised again as to the potential hazards to the fetus.

**Nursing Mothers:** A small amount of pravastatin is excreted in human breast milk. Because of the potential for serious adverse reactions in nursing infants, women taking PRAVACHOL should not nurse (see CONTRAINDICATIONS).

**Pediatric Use:** Safety and effectiveness in individuals less than 18 years old have not been established. Hence, treatment in patients less than 18 years old is not recommended at this time. (See PRECAUTIONS: General.)

**ADVERSE REACTIONS**

Pravastatin is generally well tolerated, adverse reactions have usually been mild and transient. In 4-month long placebo-controlled trials, 1.7% of pravastatin-treated patients and 1.2% of placebo-treated patients were discontinued from treatment because of adverse experiences attributed to study drug therapy, this difference was not statistically significant. In long-term studies, the most common reasons for discontinuation were asymptomatic serum transaminase increases and mild, non-specific gastrointestinal complaints. During clinical trials the overall incidence of adverse events in the elderly was not different from the incidence observed in younger patients.

**Adverse Clinical Events:** All adverse clinical events (regardless of attribution) reported in more than 2% of pravastatin-treated patients in the placebo-controlled trials are identified in the table below, also shown are the percentages of patients in whom these medical events were believed to be related or possibly related to the drug.

Body System/Event*	All Events %		Events Attributed to Study Drug %	
	Pravastatin (N = 900)	Placebo (N = 411)	Pravastatin (N = 900)	Placebo (N = 411)
Cardiovascular				
Cardiac Chest Pain	4.0	3.4	0.1	0.0
Dermatologic				
Rash	4.0*	1.7	1.3	0.9
Gastrointestinal				
Nausea/Vomiting	7.3	7.1	2.9	3.4
Diarrhea	6.2	5.6	2.0	1.9
Abdominal Pain	4.4	6.9	2.0	3.9
Constipation	3.3	2.7	2.4	5.1
Flatulence	3.3	3.8	2.4	3.4
Heartburn	2.9	1.9	2.0	0.7
General				
Fatigue	3.6	3.4	1.9	1.0
Chest Pain	3.7	0.3	0.2	0.2
Influenza	2.4*	0.0	0.0	0.0
Musculoskeletal				
Localized Pain	10.0	9.0	1.4	1.5
Myalgia	2.7	1.0	0.6	0.0
Nervous System				
Headache	6.2	3.9	1.7*	0.2
Dizziness	3.3	3.2	1.0	0.5
Renal/Genitourinary				
Urinary Abnormality	2.4	2.9	0.7	1.2
Respiratory				
Common Cold	7.0	6.3	0.0	0.0
Rhinitis	4.0	4.1	0.1	0.0
Cough	2.6	1.7	0.1	0.0

\*Statistically significantly different from placebo.

The following effects have been reported with drugs in this class:

**Skeletal:** myopathy, rhabdomyolysis.

**Neurological:** dysfunction of certain cranial nerves (including alteration of taste, impairment of extra-ocular movement, facial paresis), tremor, vertigo, memory loss, paresthesia, peripheral neuropathy, peripheral nerve palsy.

**Hypersensitivity Reactions:** An apparent hypersensitivity syndrome has been reported rarely which has included one or more of the following features: anaphylaxis, angioedema, lupus erythematosus-like syndrome, polymyalgia rheumatica, vasculitis, purpura, thrombocytopenia, leukopenia, hemolytic anemia, positive ANA, ESR increase, arthritis, arthralgia, urticaria, asthenia, photosensitivity, fever, chills, flushing, malaise, dyspnea, toxic epidermal necrolysis, erythema multiforme, including Stevens-Johnson syndrome.

**Gastrointestinal:** pancreatitis, hepatitis, including chronic active hepatitis, cholestatic jaundice, fatty change in liver, and, rarely, cirrhosis, fulminant hepatic necrosis, and hepatoma, anorexia, vomiting.

**Reproductive:** gynecostasia, loss of libido, erectile dysfunction.

**Eye:** progression of cataracts (lens opacities), ophthalmoplegia.

**Laboratory Test Abnormalities:** Increases in serum transaminase (ALT, AST) values and CPK have been observed (see WARNINGS).

Transient, asymptomatic eosinophilia has been reported. Eosinophil counts usually returned to normal despite continued therapy. Anemia, thrombocytopenia, and leukopenia have been reported with other HMG-CoA reductase inhibitors.

**Concomitant Therapy:** Pravastatin has been administered concurrently with cholestyramine, colestipol, nicotinic acid, probucol and gemfibrozil. Preliminary data suggest that the addition of either probucol or gemfibrozil to therapy with lovastatin or pravastatin is not associated with greater reduction in LDL-cholesterol than that achieved with lovastatin or pravastatin alone. No adverse reactions unique to the combination or in addition to those previously reported for each drug alone have been reported. Myopathy and rhabdomyolysis (with or without acute renal failure) have been reported when another HMG-CoA reductase inhibitor was used in combination with immunosuppressive drugs, gemfibrozil, erythromycin, or lipid-lowering doses of nicotinic acid. Concomitant therapy with HMG-CoA reductase inhibitors and these agents is generally not recommended (See WARNINGS: Skeletal Muscle and PRECAUTIONS: Drug Interactions.)

**OVERDOSAGE**

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## SCIENTIFIC ARTICLES

- American College of Surgeons, Mississippi Chapter, Fall Clinical Meeting:  
Abstracts For Presentation 335

- Clinicopathologic Conference III 346  
*Joe C. Files, MD, Editor, et al*

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## SPECIAL ARTICLE

- Certified Rural Health Clinics Increase  
Available Health Care 352

## EDITORIALS

- Snowflakes 354  
*Don Q. Mitchell, MD*  
"Details, Details" 355  
*Lee England, MD, Associate Editor*

## DEPARTMENTS

- Comment 357  
Medical Organization 360  
Personals 369  
Placement Service 375  
Classified 376

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## Clinton Health Reform Plan... What It Means for Patients

Earlier this year, the AMA developed a list of ten questions which your patients should be asking about health care reform. The following answers are based on the administration's plan as presented on September 22.

Health system reform is being developed in two stages: President Clinton has made his preliminary recommendations and now the Congress debates and develops legislation.

**1. Will I still be able to see my own doctor? Will I have to pay extra? And will my doctor and I be free to decide how to treat my illness?**

You will be able to see your doctor if you choose a plan your doctor is in. If you want to see a physician outside your plan, you will pay more and in some cases it may be the entire amount.

Your health plan may be pressed to meet government budget targets. Some plans may put economic interests ahead of medical interests. Treatment guidelines used by such plans may not be those developed by the medical profession. This could interfere with the choice of you and your doctor.

**2. I have a group insurance policy through my employer. Will that change? Will my premiums, deductibles and copayments go up?**

There will be some changes in how you get your health insurance.

The primary role for your employer will be to pay part of the premium for your plan, typically 80%. If you choose a plan that costs more than average, your share will be more than 20%.

Although all plans will offer standard coverage, if you choose a health plan that gives you a wider choice of physicians, other health professionals, and hospitals, your premium, deductibles and copayments may be higher than if you choose a plan more restricted in its choices.

**3. Will I be able to choose my own type of health insurance? And can I buy extra insurance if I want it?**

A government approved "health alliance" will decide which health plans are available for you to choose from. You will have a choice of at least three types of plans, which is more than is currently offered to some employees. You can buy extra insurance, although its cost may not be tax deductible.

(continued)

**4. Will anything be done to reduce and simplify all the insurance forms I have to fill out?**

Yes, insurance paperwork will become simpler, although there will be new rules about regional enrollment periods, the type of insurance plans you can choose from, and how much you pay based on which health plan you choose. This information is supposed to be presented to you in easily understood terms.

Everyone will be assigned a unique identification number, which will be on your own health card. There will be a central collection of patient information, which raises privacy concerns that need to be addressed.

**5. If I change jobs, get sick or am injured, will I risk losing health insurance coverage?**

You will not lose your insurance or have it reduced because you are fired or laid off, or because you quit to look for a better job. If you are self-employed or unemployed, you will be required to pay your share of the premium as well as the employer share, unless you qualify for government assistance. If you are terminated by a large employer (over 5,000 employees), your employer's obligation to continue to pay may exist for up to 6 months.

**6. What if someone in any family has a preexisting health condition. Will they be covered?**

As the AMA has been calling for for years, the proposal provides that you and your family can not be turned down for insurance, dropped or forced to pay a higher premium than others in your plan, even if you or a member of your family has AIDS, cancer or some other "preexisting condition." Nor will you have to pay a higher insurance premium because of an illness or injury unless you switch to a higher cost plan because you want more freedom of choice of physician or other provider.

**7. Will the quality of care my family receives be maintained under a new system? Will my physician's duty to put my interests first change?**

Doctors have an historic ethical duty to put patient needs above their own financial interest, to provide patients with a choice of treatments, and to fight for the best appropriate care. In the President's preliminary plan, doctors would face financial limits on the amount of care they provide. Under the rules of many plans, physicians will be given financial incentives to provide less care.

Currently, our high quality medical care is the result of private innovation that educates the world's best doctors and strives for patient satisfaction. Under the proposed system, new layers of government will play an increased role that will restrict private initiatives. Restrictions will be imposed by a new national health board, the federal government, a new government-run council on graduate medical education, state governments, and the state-regulated alliances. Additionally, many health plans may have economic pressures to hold down the use of health services. Actions by any of these bodies may limit your ability to receive, and your physician's ability to give you, what is considered the best quality medical care.

**8. I'm retired and on a fixed income. Will my Medicare coverage be affected?**

Yes, while the scope of your Medicare benefits will remain the same, proposed severe Medicare cuts may compromise your ability to receive those benefits.

If your state chooses, and has federal permission, you may be required to receive your Medicare benefits through a health alliance. If your state establishes a single-payor system, and has federal permission, you may be required to receive your health care through that system.

There will be a new Medicare benefit covering outpatient prescription drugs, with Medicare beneficiaries paying part of the cost and with the federal government having power to limit your access to designated types of specific drugs. Medicare premiums will increase for individuals with income over \$100,000 and for couples with income above \$125,000.

**9. Will costs be controlled in a way that doesn't interfere with my medical care?**

Cost controls may decrease your ability to choose and get some kinds of medical services. A national budget limit for health care will be set. The government will restrict premium increases. This may lead to rationing.

Health plans will be pressured to control costs. As a result, health plans may question your need

*(continued)*



for certain treatments, limit the types of care you can receive, delay needed care, or require a nonphysician before you're allowed to see a doctor.

This also means that hospitals and physicians will have less money to replace old equipment, to invest in new medical technology, and to try new approaches to giving you medical care.

**10. Will everybody in America have health insurance? And if so, how will we pay for this?**

Every legal resident will have health insurance. And everyone will be required to contribute to their coverage.

The preliminary proposal would have the new system financed by severe cuts in Medicare and Medicaid, insurance premiums, and sin taxes. It is very likely that these will not generate enough money to cover the expenses of the new system.

The new system will have added costs. About 37 million more Americans will have health insurance; government taxes will be needed to subsidize insurance for many of these people. In addition, there will be new administrative costs for numerous state and federal government agencies that will create and administer the new rules. In response to these new costs, additional new taxes will be required.

\*\*\*

## **Medicaid Managed Care Test Program Ready For Washington County**

Jackson, MS — A new pilot program could provide more consistent and cost-effective care for Mississippi Medicaid patients.

HEALTHlink is the name the Mississippi Medicaid division is giving to the effort that, beginning Oct. 1, will be offered in seven counties over the next two years.

The program is a form of managed care, designed to keep costs as physicians work with insurance companies to standardize fees and lower consumer's bills.

"HEALTHlink is a managed care program that allows Medicaid recipients to select a primary-care provider on their own from a pool of physicians recruited in each county," said Barry Bounds, systems analyst for the Medicaid managed-care office in Jackson.

About 3,800 Washington County Medicaid recipients have pre-enrolled in the pilot, fashioned after successful experiments in Kentucky and North Carolina. In Washington County, 10 physicians by November 1 will serve clients.

If it succeeds there, the other six counties will adopt it on a staggered basis through 1994. Participating counties will target women and children on Medicaid. More than 30,000 could benefit.

"This will give a patient consistency of care because rather than going to multiple doctors, they will go to one primary care physician, who can maintain a patient's records and send test results to other referred physicians to avoid duplication of costly procedures," Bounds said.

Bounds and Dr. Alfio Rausa, state District Health Officer for the Delta Hills Region that includes Washington County, share a dollar-saving hope: If a physician can earn trust, Medicaid patients will likely make fewer unnecessary visits to crowded emergency rooms. Instead patients will call their physicians about how to handle problems that arise.

\*\*\*

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# American College of Surgeons Mississippi Chapter Fall Clinical Meeting

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## Abstracts For Presentation

**T**he Fall Clinical Meeting of the Mississippi Chapter of the American College of Surgeons will be held in Jackson on November 19 and 20, 1993. It will take place in conjunction with both the ACS Region IV Resident's Competition for Trauma Papers and a special meeting sponsored by the Cancer Liaison Committee of the Mississippi Chapter.

The meeting will begin with a reception and banquet on Friday, November 19th, at The Cabot Lodge on North State Street. Dr. John Tarpley, a Mississippi native and a medical missionary from Ogbomosh, Nigeria, with a varied and unique surgical experience in trauma and oncology, will give an overview of surgery in the tropics at the banquet.

On Saturday, November 20th, there will be a full day of clinical presentations at The Cabot Lodge. In addition, a concurrent session of trauma papers will be held Saturday morning.

A luncheon presentation on Saturday will be made by Dr. Richard J. Field, Jr., Regent of the American College of Surgeons, on "Perspectives from the College on the Clinton Health Plan". Dr. Dana Andersen, Professor of Surgery and Medicine, at the University of Chicago Hospital, will be the guest lecturer Saturday afternoon and will discuss "Islet Cell Tumors of the Pancreas."

With ample time for questions and discussion, the format of the meeting offers the opportunity for physicians throughout the state to share their experiences and opinions. All members of the Chapter are encouraged to attend and to participate in this exchange of information. The program

agenda is listed on page 342 of this issue. Following are the abstracts of the papers which will be presented during this MS Chapter, ACS Fall Clinical Meeting.



### LOBULAR BREAST CANCER

Lobular breast cancer comprises ten per cent of all breast cancer cases. The accurate clinical diagnosis and staging of all types of breast cancer determines the appropriate treatment programs. The early diagnosis of lobular breast cancer (LBC) will be shown to be more difficult than other types of breast cancer. A review of two hundred LBC cases will be used in this study. A review of the literature revealed a range of ten to fifty per cent inability to diagnosis LBC by the use of mammogram. Twenty-five per cent of the study cases revealed no mammographic evidence of any abnormality. The various mammographic presentations of the positive cases will be discussed. Asymmetrical densities, architectural changes, microcalcifications, stellate lesions can be seen in LBC. The physical exam often failed to estimate the extent of the disease and thus the tumor would be understaged. The pathologic stage of LBC was frequently higher than the clinical stage.

William J. Gibson, Jr., MD  
Jackson, MS



## GASTRIC CARCINOMA IN MISSISSIPPI

While gastric cancer in the United States appears to be decreasing in incidence and occurring in primarily older individuals, a twelve year retrospective review of the University of Mississippi Medical Center, Jackson VA Medical Center experience (1977 - 1989) has identified a disproportionate number of gastric cancers in the predominantly younger black population. Ninety-seven patients with gastric adenocarcinoma were identified with a mean age at diagnosis of 58 years (range 22 - 84 years). There were 54 men (56%) and 43 women (44%). Seventy-eight (80%) were black while 17 (18%) were white with one American Indian and one Mexican American identified. Fifty-two patients (54%) had stage IV disease at time of diagnosis. Fifty-two patients (54%) were less than 60 years old at diagnosis and 45 (86%) were black men. The reason for this unusual age distribution for gastric carcinoma in the Mississippi population is unknown however, a combination of environmental factors and an unusually susceptible population may be involved. Archival materials are presently being collected and stored in the Molecular Surgery Laboratory, Section of Surgical Oncology, University of Mississippi Medical Center for future genetic analysis. However, at this time, the identification of a gastric ulcer in this cohort warrants careful follow-up and appropriate treatment.

Terrence J. Hall, MD  
Judy Moulder, MD  
Henry Hsu, MD  
James Achord, MD  
Carol Scott-Conner, MD  
Jackson, MS



## LEIOMYOSARCOMA OF THE ANUS: A CASE REPORT AND REVIEW OF THE LITERATURE

Leiomyosarcoma of the anus is a rare tumor initially reported by Wolfson and Oh in 1977. Since that time only six other cases have been reported in the literature. The authors report the eighth such case of this unusual soft tissue sarcoma and review of the available data concerning anorectal leiomatous tumors. These tumors typically present with a perianal mass and most frequently initial treatment has consisted of local excision or enucle-

ation despite the tendency of these lesions to local infiltration. Early lesions may lack pathologic criteria for malignancy, but a majority nonetheless recur as a higher grade of frank sarcoma. Such higher grade lesions are more likely to be associated with metastasis. Local control clearly can only be achieved by wide excision with clear margins. We therefore recommend en-bloc surgical extirpation of these tumors at an early stage of their evolution when histological criteria for malignancy may be minimal, or when clinical characteristics of aggressive behavior are present.

Mark H. Craig, MD  
Carl J. Hauser, MD  
Jackson, MS



## FAMILIAL JUVENILE POLYPOSIS: A STUDY OF A MISSISSIPPI KINDRED WITH IMPLICATIONS FOR SURGICAL MANAGEMENT

Familial juvenile polyposis (FJP) is a rare condition that is inherited as an autosomal dominant trait. One of several polyposis syndromes, it is associated with an increased risk of gastrointestinal malignancy. A kindred with FJP was identified five years ago and is under study at UMC. Of 34 living members, 15 have been investigated and histologically typical juvenile polyps found in eleven. In all cases, these were most numerous in the right colon, with few polyps in the descending colon and none in the rectum. Eight patients have had subtotal colectomies with ileorectal anastomoses. In addition to juvenile polyps, polyps with adenomatous or villous elements were identified in three of these patients; one of these patients had invasive adenocarcinoma in a large mixed polyp of the cecum. Two patients with polyps had coexisting gastric cancer.

All patients have been followed with periodic upper and lower gastrointestinal endoscopy. Polyps have recurred in the rectal remnants of three patients at a mean of 36 months after surgery. One patient has undergone conversion to total proctocolectomy with ileoanal anastomosis and J pouch. Despite the preponderance of right-sided polyps at initial diagnosis, the rapid recurrence of polyps after subtotal colectomy argue in favor of proctocolectomy at time of initial presentation.

Carol E. H. Scott-Conner, MD  
Terrence J. Hall, MD



**Deborah S. Skelton, MD  
Beverly L. Anglin, RN, CNOR  
Charu Subramony, MD  
Jackson, MS**

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### **RADICAL PROSTATECTOMY AND RADIATION THERAPY FOR LOCALIZED PROSTATE CANCER: TREATMENT OUTCOME IN 347 CONSECUTIVE PATIENTS**

The relative efficacy of radical prostatectomy (RP) and radiation therapy (RT) for the treatment of clinical stage A<sub>2</sub> and B prostate cancer, and the benefit of RT for the treatment of clinical stage C prostate cancer, are poorly defined and controversial. To provide further insights into these issues we conducted a retrospective analysis of 347 consecutive patients with localized prostate cancer who were treated with RP or RT at one institution between 1980 and 1991. During this period RP was generally recommended for men with stage A<sub>2</sub>-B tumors who had an anticipated life expectancy of > 10 years. Patients with stage A<sub>2</sub>-B tumors who were not surgical candidates and patients with stage C tumors were treated with RT. The median follow-up was 56 mos. (range 2-159 mos.). Two patients treated by RP and three treated by RT were lost to follow-up. The remaining patients have expired of known cause or were evaluated within the past six months. Actuarial curves for the various groups were calculated by the Kaplan and Meier method and the significance of differences between curves was assessed by the generalized Wilcoxon test of Gehan. 125 men with stage A<sub>2</sub>-B tumors were treated by RP and 139 were treated with RT. 83 men with stage C tumors were treated with RT. The disease free survival and cause specific survival was better among the patients with stage A<sub>2</sub>-B tumors treated by RP than by RT, but the differences were not statistically significant,  $p = .10$  and  $.21$ , respectively. The five and ten year disease free survival in the RP and RT patients with stage A<sub>2</sub>-B tumors was .85 and .80, and .63 and .51, respectively. Among the stage C patients treated with RT the five and ten year disease free survival was .39 and .05, respectively. The pretreatment PSA level (<4, 4-10 and >10 ng/ml) in both the RP and RT groups correlated directly with disease free survival, .00002 and .006, respectively. These data demonstrate that RP is marginally superior to RT

for the treatment of stage A<sub>2</sub>-B tumors but that RT is not particularly effective for the treatment of stage C tumors. The degree of PSA elevation has adverse prognostic significance in men with localized prostate cancer who are treated with RP or RT.

**Jackson E. Fowler, Jr., MD  
Nicholas T. Braswell, MD  
Jackson, MS**

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### **ANDROGEN DEPRIVATION THERAPY FOR LOCALIZED PROSTATE CANCER**

Radical prostatectomy is considered by many authorities as the treatment of choice for men with clinical stage A<sub>2</sub> and B prostate cancer if the patient has an anticipated life expectancy of >10 years. Radiation therapy is often recommended for patients with stage A<sub>2</sub>-B cancer who are not surgical candidates and for patients with stage C cancer. A recent analysis of 222 patients with localized prostate cancer who were treated with radiation therapy at our institution demonstrated overall 5 and 10 year survivals of 56% and 24%, respectively. The 5 and 10 year disease free survivals of patients with stage C tumors was 38% and 5%, respectively.

Since 1991 we have recommended androgen deprivation therapy by means of orchiectomy or LHRH agonist treatment for men with localized prostate cancer who are not candidates for radical prostatectomy. 167 patients have been treated between March, 1991 and June, 1993, and 85 patients have been followed for > 12 months. In all patients there was prompt regression of the PSA level with a mean half life of 18 days. The size of the prostate gland decreased by an average of 63% of baseline after 3 months of treatment and by an average of 44% of baseline after 21 months of treatment. No patients have had clinically demonstrable tumor progression although 5 have had elevation of the PSA level. This ongoing treatment experience, which will be presented in more detail, should help to define the role of androgen deprivation therapy in the management of localized prostate cancer.

**Jackson E. Fowler, Jr., MD  
Nicholas T. Braswell, MD  
Linda Seaver, MD  
Prabhakar Pandey, MD  
Jackson, MS**

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## SELECTIVE USE OF LAPAROSCOPY IN THE PATIENT WITH ADVANCED MALIGNANCY

We recently reviewed our initial experience (February 1, 1990 through March 31, 1993) of selectively utilizing laparoscopy in the diagnosis and palliation of advanced malignancy. A total of 96 laparoscopic or open abdominal operations for malignancy were performed during the study period. Laparoscopy was performed in 21 patients (22%). Diagnostic laparoscopy with biopsy was performed in all, nine patients had additional palliative laparoscopic procedures. Of the 12 patients having purely diagnostic laparoscopy, nine subsequently underwent laparotomy and major resection (7 patients) or palliative procedure (2 patients). Three patients with disseminated disease but no clinical obstruction underwent laparoscopy and biopsy only.

Palliative laparoscopic procedures (5 gastrostomies, 2 ileostomies, 1 colostomy, and 1 laparoscopic-assisted gastrojejunostomy) were performed in nine patients. Extracorporeal suturing and knot-tying simplified these procedures. Mean operative time was 65 minutes (range 55 to 100). One complication (prolapse of loop colostomy requiring local revision) occurred 4 weeks after laparoscopy. Four patients are alive at 5.6 months (range 3 to 7.4) months after laparoscopic palliation, five have died (mean survival 3.9 months).

Review of the patients in whom laparoscopy was not performed revealed 22 in whom it might have altered the management by providing diagnostic information or palliation. The remaining 53 patients (52%) underwent major resections for palliation or cure.

Laparoscopy provided confirmation of extent of disease in 20 patients (one was understaged) and satisfactory long-term palliation in nine. Selective laparoscopy can be a useful adjunct in cancer patients with a limited life expectancy and no hope of cure, and does not necessarily require "advanced" laparoscopic skills.

A. R. Thompson, MD  
T. J. Hall, MD  
F. F. Maukkassa, MD  
B. A. Anglin, RN, CNOR  
J. T. Moulder, RRT  
C. E. H. Scott-Conner, MD  
Jackson, MS



## CURRENT STATE OF LAPAROSCOPY IN UROLOGY

With the current advances in laparoscopy equipment and laparoscopic experience by urologists, the number of surgical procedures suitable for laparoscopic intervention has increased dramatically. Initial use of laparoscopy in urology involved its utilization for localization of a nonpalable testis. However, only a small number of urologic surgeons were performing this procedure. With the development of laparoscopic pelvic lymphadenectomy, the number of laparoscopic procedures being undertaken increased dramatically. With the large number of patients being diagnosed with early stage carcinoma of prostate, the opportunity is present for these patients to undergo a laparoscopic lymph node dissection. Recent advances in laparoscopic stapling and suturing has allowed urologic surgeons to perform laparoscopic nephrectomies, prostatectomies and cystectomies. A review of current laparoscopic procedures and applications in urology will be presented.

W. Bruce Shingleton, MD  
Jackson E. Fowler, Jr., MD  
Jackson, MS



## LAPAROSCOPIC INGUINAL HERNIORRHAPHY: INITIAL EXPERIENCE IN A COMMUNITY HOSPITAL

Since February 1992, 32 laparoscopic herniorrhaphies have been performed in 25 patients, including 15 indirect, 16 direct and 1 femoral defect. These were performed in a 275 bed community hospital initially using a "plug and patch" technique, and later employing repair of the hernia defect with a sheet of prolene mesh only. Patients were managed on an out patient basis and were able to resume full activity in 7 to 10 days. Despite the lack of long term follow-up and additional cost basis for the laparoscopic procedure, this method of repairing hernia defects promises to be safe and effective with a high degree of patient satisfaction.

Bruce Pruett, M.D.  
Laurel, MS





## EARLY REPORT OF 100 INGUINAL HERNIA REPAIRS BY LAPAROSCOPIC APPROACH

100 consecutive inguinal hernia repairs were done using the laparoscopic approach. The repair was a "Stoppa" preperitoneal prosthetic repair using Marlex. Initially a Marlex plug was also used, but has been abandoned. Patient population is analyzed by gender, age and type of hernia. Ninety-five percent follow-up has been achieved and results will be presented. Discussion of preperitoneal prosthetic inguinal hernia is presented.

W. P. Kennerly, MD  
Biloxi, MS

Donald J. Booth, MD  
Ocean Springs, MS

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## VARIABLE COSTS FOR LAPAROSCOPIC CHOLECYSTECTOMY IN MISSISSIPPI

The hospital charge for laparoscopic cholecystectomy (from published reports within the surgical literature) varies across the USA with the lowest published charge coming from Jackson, MS. Recent studies have now been completed to determine differences in hospital charges for cholecystectomy across Mississippi. In an effort to explain the surgeon's role in increasing the patient's hospital bill, an in-hospital study was performed to correlate the surgeon's choice of instrumentation with the hospital charge for OR services.

Part 1: A major insurer was asked to collect data from each of the larger hospitals in Mississippi. To avoid variance explained by complications or graded illness, only those patients were included that were (a) less than 65 years of age and (b) hospitalized less than 48 hours. Our purpose was to develop the "core costs" for the procedure at each facility. Average reimbursements were compared for each hospital.

MS Baptist Hospital	2472
St. Dominic	2813
Hattiesburg	3964
Tupelo	4269

The trend was also identified from total charges submitted to Medicare by DRG for patients greater than 69 years of age.

Hospital	Mean Total Charge	#Patients
MS Baptist	5,275	106
St. Dominic	7,742	57
Hattiesburg	12,146	58
Tupelo	9,478	121

Part II: An in-hospital study of 300 laparoscopic cholecystectomies was performed. The total hospital charge submitted to the patient for OR services was completed; additional charges related to prolonged OR time were excluded. OR times from patient entry into the room until exit were tabulated.

Surgeon	Avg time	#Cases	OR charge excl. time
A	65	129	1126
B	61	113	1312
C,D	84	20-40	1527
E-L	100	4-19	1662
M	120	1	3777

Lower costs and shorter OR times were associated with increasing caseload and reusable instruments. In this analysis, the use of disposable instruments correlated directly with longer OR times in addition to charges.

CONCLUSIONS: The hospital charge for laparoscopic cholecystectomy varies markedly across the state and within each hospital according to surgeon. The primary determinant of increased charges appears to be the use of disposable instruments. Any potential benefit of disposable instruments - excluding enhanced hospital revenue - was not apparent in this review.

RECOMMENDATIONS: The Mississippi Chapter of the American College of Surgeons should support programs to assure fiscal responsibility of our most common abdominal operation. Our efforts should serve as a model for the rest of the United States.

C. Randle Voyles MD  
D. L. Sanders, BS  
Jackson, MS

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## FINE NEEDLE ASPIRATION (FNA) OF PAROTID MASSES

Fine needle aspiration is a technique which has a wide range of applications in the region of the head and neck. The present study was undertaken

to evaluate the efficacy of fine needle aspiration in patients presenting with parotid masses.

Twenty-five consecutive patients who were referred for evaluation of parotid masses constitute the study group. This group was evaluated in terms of the diagnostic accuracy of fine needle aspiration. The sensitivity of fine needle aspiration was 92%. Specificity was 96%. This finding is consistent with previously reported series.

Fine needle aspiration plays a significant role in management of parotid masses. The patient can be advised in an expeditious manner if they have a problem which will require medical or surgical treatment. Many patients may be spared consideration of surgery altogether. The technique of fine needle aspiration is demonstrated.

**C. Ron Cannon, MD  
Jackson, MS**



### **SURGICAL TREATMENT OF CAROTID BODY TUMORS**

Carotid body tumors pose complex surgical management decisions including preoperative assessment of the degree of internal carotid body involvement. Recent developments in imaging methods, methods of cerebral blood flow measurements, balloon occlusion testing, as well as techniques to maintain vascular flow when grafting is required, have resulted in improved ability to completely resect these tumors with reduced complications. These methods are discussed in the light of our experience in managing 17 carotid body tumors in fifteen patients. Intraoperative dissection of the tumor from the vessel wall, vagus and hypoglossal nerves was complicated by dense fibrotic adhesions from prior surgery in three patients. In three patients, injury to the vessel wall required appropriate surgical intervention.

**Tammy Sanders, MD  
Vinod K. Anand, MD  
Seshadri Raju, MD  
Gilberto Alemar, MD  
Jackson, MS**



### **STEREOTACTIC RADIOSURGERY OF THE BRAIN**

Radiosurgery is not a new technology, having been tested and used in Europe for the past quarter century. The original "Gamma Knife" technique was performed with a helmet loaded with hundreds of small Co<sup>60</sup> sources to create a biological lesion in three dimensional space. Recently, computer technology has allowed the development of treatment plans which use collimated linear accelerators, thereby extending the availability of this therapy to many patients. Unlike radiotherapy, the radiosurgery lesion is necrotizing and is delivered in a single session using many arcs and beams to produce sharply defined lesions in the organ treated.

As of June 1993, 30 patients have been treated at the University Hospital using the "X-Knife", a commercial software and hardware package. The lesions consisted of arteriovenous malformations and of both benign and malignant brain tumors in children and adults. Radiosurgery may also be used for the treatment of pain, motor disorders, and behavioral modification.

Theoretically, this form of surgery can be extended to virtually any organ in which ablative surgery is now used. Because it can be delivered to the outpatient and is relatively noninvasive, it will be favored in the future economics of health care.

**Robert R. Smith, MD  
Jackson, MS**



### **NITRIC OXIDE: PATHOGENESIS OF ARDS**

Nitric Oxide (NO), a simple inorganic molecule, has only recently been recognized to have important regulatory and cytotoxic properties. NO stimulates vasorelaxation by activating guanylate cyclase within vascular smooth muscle, thus is an important modulator of vascular tone. In addition, macrophage produced NO has shown to be cytotoxic to intracellular organisms such as malaria, to tumor cells in vitro and to pancreatic islet cells.

Nitric Oxide is synthesized from L-arginine by two isoforms of the enzyme NO synthase (NOS). The inducible enzyme (iNOS) makes large molar amounts of NO in response to cytokines such as tumor necrosis factor- $\alpha$  (TNF $\alpha$ ),  $\gamma$ -interferon (IFN- $\gamma$ ) and *Escherichia coli* lipopolysaccharide (LPS).



Inflammatory cytokines stimulate inducible NO production in the pulmonary vasculature. These cytokines are also elevated in conditions of post-traumatic gram-negative sepsis. Such a mechanism has immediate relevance to the conditions that characterize acute lung injury and adult respiratory distress syndrome (ARDS). The mechanism by which NO injures the lung will be discussed, along with future clinical applications.

**Keith R. Thomae, MD**  
**Jackson, MS**  
**Don K. Nakayama, MD**  
**Pittsburgh, PA**



### **DIFFUSE INTRAVASCULAR THROMBOSIS AND LIMB LOSS DUE TO HEPARIN- INDUCED ANTIPLATELET ANTIBODIES**

Heparin-induced antiplatelet antibodies (HIAA) develop in approximately 5 percent of patients receiving heparin. HIAA promote platelet aggregation and may result in a heparin-induced thrombocytopenia and thrombosis (HITT) syndrome. During the past two years, we treated two patients for profound HITT. Patient 1 was a 40 year old female being treated with heparin for deep venous thrombosis secondary to iliac vein compression by massive uterine fibroids. She was referred because of progressive leg edema, cyanosis, and neurologic deficit. Thrombocytopenia was noted on admission (lowest platelet count 12,000/mm<sup>3</sup>, HIAA was confirmed by serology, an inferior vena caval filter was inserted, and she was anticoagulated with aspirin and an investigational low molecular weight heparin. Venous thrombectomy was unsuccessful. A thrombotic stroke occurred one day after admission. Patient 2 was a 67 year old female who developed thrombocytopenia (lowest platelet count 11,000/mm<sup>3</sup> and lower extremity arterial and venous thrombosis after coronary bypass grafting. HIAA was confirmed, heparin was discontinued, aspirin was administered, and an inferior vena caval filter was inserted. Arterial thrombectomy was possible, but venous thrombectomy was unsuccessful. Both patients survived after high above-knee amputation. HITT develops 5-15 days after exposure, which may be as small as that with heparin-coated intravascular catheters or heparin "flush." The platelet count is characteristically less than 100,000/mm<sup>3</sup> and rises within a few days of discontinuation of heparin. Platelet aggregation tests are positive for HIAA. There are no known genetic or other predisposing factors. Se-

vere cases result in profound thrombocytopenia, intravascular thrombosis, and rarely hemorrhagic complications. All patients receiving heparin therapy, flushes, or coated vascular catheters should have daily platelet count monitoring. A platelet count less than 100,000/mm<sup>3</sup> or heparin resistance should result in discontinuation of heparin and platelet aggregation tests for HIAA. Aspirin is helpful in preventing further platelet thrombus formation and oral anticoagulation should be instituted as soon as possible. Treatment with low-molecular weight heparin, dextran, prostacyclin analogs, fibrinolytic agents and defibrinogenating agents has demonstrated only occasional success. Diffuse small vessel platelet thrombi are resistant to surgical thrombectomy and pharmacologic thrombolysis, resulting in frequent limb loss and a mortality rate as high as 25%. Early recognition and discontinuation of heparin therapy is the most effective method of preventing the devastating complications due to HITT.

**Edward E. Rigdon, MD**  
**Jackson, MS**



### **MISSISSIPPI SNAKEBITES**

In view of the extensive forestry operations in our state, it is incredible that more difficulties have not been experienced with snakebites. Commonly seen in our timberlands are the cottonmouth moccasin, the copperhead moccasin, the rattlesnake, and occasionally the coral snake. It is a tribute to our forestry personnel and the protection they use that there is a low incidence of serious problems.

Our records here at the Field Clinic and Field Hospital regarding snakebites began in 1922, and there is no recording of a fatality. We are reviewing the hospitalized snakebites since 1983 including the degree of envenomation complications and morbidities thereof. Our method of immediate treatment will be depicted which involves excision of the skin and subcutaneous tissues at the site of the fang marks. This has been a most successful method which was begun several years ago following a presentation on snakebites at the Mississippi State Medical Association Meeting in Biloxi.

**Richard J. Field, Jr., MD,**  
**Richard J. Field, III, MD,**  
**Centreville, MS**

**Fall Clinical Meeting**  
**American College of Surgeons**  
**Mississippi Chapter**  
**November 20, 1993 • Jackson, MS • Cabot Lodge**

8:00 am     Coffee  
 8:25 am     Welcoming Remarks — Charles S. O'Mara, MD

**Morning Paper Session #1: CURRENT TOPICS IN CANCER SURGERY**

8:30 am     ***Lobular Breast Carcinoma***  
                  William J. Gibson, Jr., MD  
 8:45 am     ***Gastric Carcinoma in Mississippi***  
                  Terrence J. Hall, PhD, MD; Judy Moulder, MD; Henry Hsu, MD; James Achord,  
                  MD; Carol Scott-Conner, MD, PhD  
 9:00 am     ***Leiomyosarcoma of the Anus: A Case Report and Review of the Literature***  
                  Mark H. Craig, MD; Carl J. Hauser, MD  
 9:15 am     ***Familial Juvenile Polyposis: A Study of Mississippi Kindred with Implications***  
                  ***for Surgical Management***  
                  Carol E. H. Scott-Conner, MD, PhD; Terrence J. Hall, PhD, MD; Deborah S.  
                  Skelton, MD; Beverly L. Anglin, RN, CONR; Charu Subramony, MD  
 9:30 am     ***Current Treatment of Localized Prostate Cancer***  
                  Jackson E. Fowler, Jr., MD  
 10:00 am     Coffee Break

**Morning Paper Session #2: SELECTED TOPICS IN LAPAROSCOPIC SURGERY**

10:15 am     ***Selective Use of Laparoscopy in the Patient with Advanced Malignancy***  
                  A. R. Thompson, MD; T. J. Hall, PhD, MD; F. F. Maukkassa, MD; B.A. Anglin,  
                  RN, CNOR; J. T. Moulder, RRT; C.E.H. Scott-Conner, MD, PhD  
 10:30 am     ***Current State of Laparoscopy in Urology***  
                  W. Bruce Shingleton, MD; Jackson E. Fowler, Jr., MD  
 10:45 am     ***Laparoscopic Inguinal Herniorrhaphy: Initial Experience in a***  
                  ***Community Hospital***  
                  Bruce Pruett, MD  
 11:00 am     ***Early Report of 100 Inguinal Hernia Repairs by Laparoscopic Approach***  
                  W.P. Kennerly, MD; Donald J. Booth, MD  
 11:15 am     ***Variable Costs for Laparoscopic Cholecystectomy in Mississippi***  
                  C. Randle Voyles, MD; D. L. Sanders, BS  
 11:30 am     ***Laparoscopy Panel Discussion: Robert S. Rhodes, MD — Moderator***  
                  Drs. Thompson, Shingleton, Pruett, Kennerly, Voyles  
 Noon         Luncheon — ***Perspectives from the American College of Surgeons on the***  
                  ***Clinton Health Plan***  
                  Richard J. Field, Jr., MD, Regent, ACS



- 1:30 pm     **Guest Lecture — *Islet Cell Tumors of the Pancreas***  
Dana K. Andersen, MD, Professor of Surgery and Medicine,  
University of Chicago Hospital

**Afternoon Paper Session**

- 2:30 pm     ***Fine Needle Aspiration (FNA) of Parotid Masses***  
C. Ron Cannon, MD
- 2:45 pm     ***Surgical Treatment of Carotid Body Tumors***  
Tammy Sanders, MD; Vinod K. Anand, MD; Seshadri Raju, MD; Gilberto Alemar, MD
- 3:00 pm     ***Stereotactic Radiosurgery of the Brain***  
Robert R. Smith, MD
- 3:15 pm     ***Nitric Oxide: Pathogenesis of ARDS***  
Keith R. Thomae, MD; Don K. Nakayama, MD
- 3:30 pm     ***Diffuse Intravascular Thrombosis and Limb Loss Due to Heparin-Induced Antiplatelet Antibodies***  
Edward E. Rigdon, MD
- 3:45 pm     ***Mississippi Snakebites***  
Richard J. Field, III, MD; Richard J. Field, Jr., MD

**Closing Remarks**

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**USE IN PREGNANCY:** When used in pregnancy during the second and third trimesters, ACE inhibitors can cause injury and even death to the developing fetus. When pregnancy is detected, Vaseretic® (Enalapril Maleate-Hydrochlorothiazide) should be discontinued as soon as possible. See WARNINGS, Fetal/Neonatal Morbidity and Mortality.

**VASERETIC® 10-25**  
Enalapril Maleate-Hydrochlorothiazide

*Next*

Dosage must be individualized; the fixed combination is not for initial therapy.

Evaluation of the hypertensive patient should always include assessment of renal function.

For a Brief Summary of Prescribing Information, see adjacent pages.



**TABLETS  
VASERETIC®  
(ENALAPRIL MALEATE-HYDROCHLOROTHIAZIDE)**

**USE IN PREGNANCY:** When used in pregnancy during the second and third trimesters, ACE inhibitors can cause injury and even death to the developing fetus. When pregnancy is detected, VASERETIC® (Enalapril Maleate-Hydrochlorothiazide) should be discontinued as soon as possible. See WARNINGS, Fetal/Neonatal Morbidity and Mortality.

**CONTRAINDICATIONS:** VASERETIC is contraindicated in patients who are hypersensitive to any component of this product and in patients with a history of angioedema related to previous treatment with an angiotensin converting enzyme inhibitor. Because of the hydrochlorothiazide component, this product is contraindicated in patients with anuria or hypersensitivity to other sulfonamide-derived drugs.

**WARNINGS:** General: Enalapril Maleate: Hypotension: Excessive hypotension was rarely seen in uncomplicated hypertensive patients but is a possible consequence of enalapril use in severely salt/volume depleted persons such as those treated vigorously with diuretics or patients on dialysis.

Syncope has been reported in 1.3 percent of patients receiving VASERETIC. In patients receiving enalapril alone, the incidence of syncope is 0.5 percent. The overall incidence of syncope may be reduced by proper titration of the individual components. (See PRECAUTIONS, Drug Interactions, and ADVERSE REACTIONS.)

In patients with severe congestive heart failure, with or without associated renal insufficiency, excessive hypotension has been observed and may be associated with oliguria and/or progressive azotemia, and rarely with acute renal failure and/or death. Because of the potential fall in blood pressure in these patients, therapy should be started under very close medical supervision. Such patients should be followed closely for the first two weeks of treatment and whenever the dose of enalapril and/or diuretic is increased. Similar considerations may apply to patients with ischemic heart or cerebrovascular disease, in whom an excessive fall in blood pressure could result in a myocardial infarction or cerebrovascular accident.

If hypotension occurs, the patient should be placed in the supine position and, if necessary, receive an intravenous infusion of normal saline. A transient hypotensive response is not a contraindication to further doses, which usually can be given without difficulty once the blood pressure has increased after volume expansion.

**Angioedema:** Angioedema of the face, extremities, lips, tongue, glottis and/or larynx has been reported in patients treated with angiotensin converting enzyme inhibitors, including enalapril. In such cases VASERETIC should be promptly discontinued and appropriate therapy and monitoring should be provided until complete and sustained resolution of signs and symptoms has occurred. In instances where swelling has been confined to the face and lips the condition has generally resolved without treatment, although antihistamines have been useful in relieving symptoms. Angioedema associated with laryngeal edema may be fatal. Where there is involvement of the tongue, glottis or larynx, likely to cause airway obstruction, appropriate therapy, e.g., subcutaneous epinephrine solution 1:1000 (0.3 mL to 0.5 mL) and/or measures necessary to ensure a patent airway, should be promptly provided. (See ADVERSE REACTIONS.)

Patients with a history of angioedema unrelated to ACE inhibitor therapy may be at increased risk of angioedema while receiving an ACE inhibitor (see also CONTRAINDICATIONS).

**Neutropenia/Agranulocytosis:** Another angiotensin converting enzyme inhibitor, captopril, has been shown to cause agranulocytosis and bone marrow depression, rarely in uncomplicated patients but more frequently in patients with renal impairment especially if they also have a collagen vascular disease. Available data from clinical trials of enalapril are insufficient to show that enalapril does not cause agranulocytosis at similar rates. Marketing experience has revealed several cases of neutropenia or agranulocytosis in which a causal relationship to enalapril cannot be excluded. Periodic monitoring of white blood cell counts in patients with collagen vascular disease and renal disease should be considered.

**Hydrochlorothiazide:** Thiazides should be used with caution in severe renal disease. In patients with renal disease, thiazides may precipitate azotemia. Cumulative effects of the drug may develop in patients with impaired renal function.

Thiazides should be used with caution in patients with impaired hepatic function or progressive liver disease, since minor alterations of fluid and electrolyte balance may precipitate hepatic coma.

Sensitivity reactions may occur in patients with or without a history of allergy or bronchial asthma.

The possibility of exacerbation or activation of systemic lupus erythematosus has been reported.

Lithium generally should not be given with thiazides (see PRECAUTIONS, Drug Interactions, Enalapril Maleate and Hydrochlorothiazide).

**Pregnancy:** Enalapril-Hydrochlorothiazide: There was no teratogenicity in rats given up to 90 mg/kg/day of enalapril (150 times the maximum human dose) in combination with 10 mg/kg/day of hydrochlorothiazide (2 1/2 times the maximum human dose) or in mice given up to 30 mg/kg/day of enalapril (50 times the maximum human dose) in combination with 10 mg/kg/day of hydrochlorothiazide (2 1/2 times the maximum human dose). At these doses, fetotoxicity expressed as a decrease in average fetal weight occurred in both species. No fetotoxicity occurred at lower doses; 30/10 mg/kg/day of enalapril-hydrochlorothiazide in rats and 10/10 mg/kg/day of enalapril-hydrochlorothiazide in mice.

When used in pregnancy during the second and third trimesters, ACE inhibitors can cause injury and even death to the developing fetus. When pregnancy is detected, VASERETIC should be discontinued as soon as possible. (See Enalapril Maleate, Fetal/Neonatal Morbidity and Mortality, below.)

**Enalapril Maleate:** Fetal/Neonatal Morbidity and Mortality: ACE inhibitors can cause fetal and neonatal morbidity and death when administered to pregnant women. Several dozen cases have been reported in the world literature. When pregnancy is detected, ACE inhibitors should be discontinued as soon as possible.

The use of ACE inhibitors during the second and third trimesters of pregnancy has been associated with fetal and neonatal injury, including hypotension, neonatal skull hypoplasia, anuria, reversible or irreversible renal failure, and death. Oligohydramnios has also been reported, presumably resulting from decreased fetal renal function; oligohydramnios in this setting has been associated with fetal limb contractures, craniofacial deformation, and hypoplastic lung development. Prematurity, intrauterine growth retardation, and patent ductus arteriosus have also been reported, although it is not clear whether these occurrences were due to the ACE-inhibitor exposure.

These adverse effects do not appear to have resulted from intrauterine ACE-inhibitor exposure that has been limited to the first trimester. Mothers whose embryos and fetuses are exposed to ACE inhibitors only during the first trimester should be so informed. Nonetheless, when patients become pregnant, physicians should make every effort to discontinue the use of VASERETIC as soon as possible.

Rarely (probably less often than once in every thousand pregnancies), no

10  
mg

25  
mg

alternative to ACE inhibitors will be found. In these rare cases, the mothers should be apprised of the potential hazards to their fetuses, and serial ultrasound examinations should be performed to assess the intraamniotic environment.

If oligohydramnios is observed, VASERETIC should be discontinued unless it is considered lifesaving for the mother. Contraction stress testing (CST), a non-stress test (NST), or biophysical profiling (BPP) may be appropriate, depending upon the week of pregnancy. Patients and physicians should be aware, however, that oligohydramnios may not appear until after the fetus has sustained irreversible injury.

Infants with histories of *in utero* exposure to ACE inhibitors should be closely observed for hypotension, oliguria, and hyperkalemia. If oliguria occurs, attention should be directed toward support of blood pressure and renal perfusion. Exchange transfusion or dialysis may be required as means of reversing hypotension and/or substituting for disordered renal function. Enalapril, which crosses the placenta, has been removed from neonatal circulation by peritoneal dialysis with some clinical benefit, and theoretically may be removed by exchange transfusion, although there is no experience with the latter procedure.

No teratogenic effects of enalapril were seen in studies of pregnant rats, and rabbits. On a mg/kg basis, the doses used were up to 333 times (in rats), and 50 times (in rabbits) the maximum recommended human dose.

**Hydrochlorothiazide:** Teratogenic Effects: Reproduction studies in the rabbit, the mouse and the rat at doses up to 100 mg/kg/day (50 times the human dose) showed no evidence of external abnormalities of the fetus due to hydrochlorothiazide. Hydrochlorothiazide given in a two-liter study in rats at doses of 4-5.6 mg/kg/day (approximately 1-2 times the usual daily human dose) did not impair fertility or produce birth abnormalities in the offspring. Thiazides cross the placental barrier and appear in cord blood.

**Nonteratogenic Effects:** These may include fetal or neonatal jaundice, thrombocytopenia, and possibly other adverse reactions which have occurred in the adult.

**PRECAUTIONS:** General: Enalapril Maleate; Impaired Renal Function: As a consequence of inhibiting the renin-angiotensin-aldosterone system, changes in renal function may be anticipated in susceptible individuals. In patients with severe congestive heart failure whose renal function may depend on the activity of the renin-angiotensin-aldosterone system, treatment with angiotensin converting enzyme inhibitors, including enalapril, may be associated with oliguria and/or progressive azotemia and rarely with acute renal failure and/or death.

In clinical studies in hypertensive patients with unilateral or bilateral renal artery stenosis, increases in blood urea nitrogen and serum creatinine were observed in 20 percent of patients. These increases were almost always reversible upon discontinuation of enalapril and/or diuretic therapy. In such patients renal function should be monitored during the first few weeks of therapy.

Some patients with hypertension or heart failure with no apparent pre-existing renal vascular disease have developed increases in blood urea and serum creatinine, usually minor and transient, especially when enalapril has been given concomitantly with a diuretic. This is more likely to occur in patients with pre-existing renal impairment. Dosage reduction of enalapril and/or discontinuation of the diuretic may be required.

**Evaluation of the hypertensive patient should always include assessment of renal function.**

**Hemodialysis Patients:** Anaphylactoid reactions have been reported in patients dialyzed with high-flux membranes (e.g., AN 69®) and treated concomitantly with an ACE inhibitor. In these patients consideration should be given to using a different type of dialysis membrane or a different class of antihypertensive agent.

**Hyperkalemia:** Elevated serum potassium (greater than 5.7 mEq/L) was observed in approximately one percent of hypertensive patients in clinical trials treated with enalapril alone. In most cases these were isolated values which resolved despite continued therapy, although hyperkalemia was a cause of discontinuation of therapy in 0.26 percent of hypertensive patients. Hyperkalemia was less frequent (approximately 0.1 percent) in patients treated with enalapril plus hydrochlorothiazide. Risk factors for the development of hyperkalemia include renal insufficiency, diabetes mellitus, and the concomitant use of potassium-sparing diuretics, potassium supplements and/or potassium-containing salt substitutes, which should be used cautiously, if at all, with enalapril. (See Drug Interactions.)

**Cough:** Cough has been reported with the use of ACE inhibitors. Characteristically, the cough is nonproductive, persistent and resolves after discontinuation of therapy. ACE inhibitor-induced cough should be considered as part of the differential diagnosis of cough.

**Surgery/Anesthesia:** In patients undergoing major surgery or during anesthesia with agents that produce hypotension, enalapril may block angiotensin II formation secondary to compensatory renin release. If hypotension occurs and is considered to be due to this mechanism, it can be corrected by volume expansion.

**Hydrochlorothiazide:** Periodic determination of serum electrolytes to detect possible electrolyte imbalance should be performed at appropriate intervals. All patients receiving thiazide therapy should be observed for clinical signs of fluid or electrolyte imbalance: hyponatremia, hypochloremic alkalosis, and hypokalemia. Serum and urine electrolyte determinations are particularly important when the patient is vomiting excessively or receiving parenteral fluids. Warning signs or symptoms of fluid and electrolyte imbalance, irrespective of cause, include dryness of mouth, thirst, weakness, lethargy, drowsiness, restlessness, confusion, seizures, muscle pains or cramps, muscular fatigue, hypotension, oliguria, tachycardia, and gastrointestinal disturbances such as nausea and vomiting.

Hyperkalemia may develop, especially with brisk diuresis, when severe cirrhosis is present, or after prolonged therapy. Interference with adequate oral electrolyte intake will also contribute to hyperkalemia. Hyperkalemia may cause cardiac arrhythmia and may also sensitize or exaggerate the response of the heart to the toxic effects of digitalis (e.g., increased ventricular irritability). Because enalapril reduces the production of aldosterone, concomitant therapy with enalapril attenuates the diuretic-induced potassium loss (see Drug Interactions, Agents Increasing Serum Potassium).

Although any chloride deficit is generally mild and usually does not require specific treatment except under extraordinary circumstances (as in liver disease or renal disease), chloride replacement may be required in the

treatment of metabolic alkalosis.

Dilutional hyponatremia may occur in edematous patients in hot weather; appropriate therapy is water restriction, rather than administration of salt, except in rare instances when the hyponatremia is life-threatening. In actual salt depletion, appropriate replacement is the therapy of choice.

Hyperuricemia may occur or frank gout may be precipitated in certain patients receiving thiazide therapy.

In diabetic patients dosage adjustments of insulin or oral hypoglycemic agents may be required. Hyperglycemia may occur with thiazide diuretics. Thus latent diabetes mellitus may become manifest during thiazide therapy. The antihypertensive effects of the drug may be enhanced in the post-sympathetic patient.

If progressive renal impairment becomes evident consider withholding or discontinuing diuretic therapy.

Thiazides have been shown to increase the urinary excretion of magnesium; this may result in hypomagnesemia.

Thiazides may decrease urinary calcium excretion. Thiazides may cause intermittent and slight elevation of serum calcium in the absence of known disorders of calcium metabolism. Marked hypercalcemia may be evidence of hidden hyperparathyroidism. Thiazides should be discontinued before carrying out tests for parathyroid function.

Increases in cholesterol and triglyceride levels may be associated with thiazide diuretic therapy.

**Information for Patients:** Angioedema: Angioedema, including laryngeal edema, may occur especially following the first dose of enalapril. Patients should be so advised and told to report immediately any signs or symptoms suggesting angioedema (swelling of face, extremities, eyes, lips, tongue, difficulty in swallowing or breathing) and to take no more drug until they have consulted with the prescribing physician.

**Hypotension:** Patients should be cautioned to report lightheadedness especially during the first few days of therapy. If actual syncope occurs, the patients should be told to discontinue the drug until they have consulted with the prescribing physician.

All patients should be cautioned that excessive perspiration and dehydration may lead to an excessive fall in blood pressure because of reduction in fluid volume. Other causes of volume depletion such as vomiting or diarrhea may also lead to a fall in blood pressure; patients should be advised to consult with the physician.

**Hyperkalemia:** Patients should be told not to use salt substitutes containing potassium without consulting their physician.

**Neutropenia:** Patients should be told to report promptly any indication of infection (e.g., sore throat, fever) which may be a sign of neutropenia.

**Pregnancy:** Female patients of childbearing age should be told about the consequences of second- and third-trimester exposure to ACE inhibitors, and they should also be told that these consequences do not appear to have resulted from intrauterine ACE-inhibitor exposure that has been limited to the first trimester. These patients should be asked to report pregnancies to their physicians as soon as possible.

**NOTE:** As with many other drugs, certain advice to patients being treated with VASERETIC is warranted. This information is intended to aid in the safe and effective use of this medication. It is not a disclosure of all possible adverse or intended effects.

**Drug Interactions:** Enalapril Maleate: **Hypotension—Patients on Diuretic Therapy:** Patients on diuretics and especially those in whom diuretic therapy was recently instituted, may occasionally experience an excessive reduction of blood pressure after initiation of therapy with enalapril. The possibility of hypotensive effects with enalapril can be minimized by either discontinuing the diuretic or increasing the salt intake prior to initiation of treatment with enalapril. If it is necessary to continue the diuretic, provide medical supervision for at least two hours and until blood pressure has stabilized for at least an additional hour. (See WARNINGS.)

**Agents Causing Renin Release:** The antihypertensive effect of enalapril is augmented by antihypertensive agents that cause renin release (e.g., diuretics).

**Other Cardiovascular Agents:** Enalapril has been used concomitantly with beta adrenergic-blocking agents, methylglucosides, calcium-channel blocking agents, hydralazine and prazosin without evidence of clinically significant adverse interactions.

**Agents Increasing Serum Potassium:** Enalapril attenuates diuretic-induced potassium loss. Potassium-sparing diuretics (e.g., spironolactone, triamterene, or amiloride), potassium supplements, or potassium-containing salt substitutes may lead to significant increases in serum potassium. Therefore, if concomitant use of these agents is indicated because of demonstrated hypokalemia they should be used with caution and with frequent monitoring of serum potassium.

**Lithium:** Lithium toxicity has been reported in patients receiving lithium concomitantly with drugs which cause elimination of sodium, including ACE inhibitors. A few cases of lithium toxicity have been reported in patients receiving concomitant enalapril and lithium and were reversible upon discontinuation of both drugs. It is recommended that serum lithium levels be monitored frequently if enalapril is administered concomitantly with lithium. **Hydrochlorothiazide:** When administered concurrently the following drugs may interact with thiazide diuretics:

**Alcohol, barbiturates, or narcotics—**potentiation of orthostatic hypotension may occur.

**Antidiabetic drugs (oral agents and insulin)—**dosage adjustment of the antidiabetic drug may be required.

**Other antihypertensive drugs—**additive effect or potentiation.

**Cholestyramine and colestipol resins—**Cholestyramine and colestipol resins bind the hydrochlorothiazide and reduce its absorption from the gastrointestinal tract by up to 85 and 43 percent, respectively. Thiazides may be administered two to four hours before the resin when the two drugs are used concomitantly.

**Corticosteroids, ACTH—**intensified electrolyte depletion, particularly hypokalemia.

**Pressor amines (e.g., norepinephrine)—**possible decreased response to pressor amines but not sufficient to preclude their use.

**Skeletal muscle relaxants, nondepolarizing (e.g., tubocurarine)—**possible increased responsiveness to the muscle relaxant.

**Lithium—**should not generally be given with diuretics. Diuretic agents reduce the renal clearance of lithium and add a high risk of lithium toxicity. Refer to the package insert for lithium preparations before use of such preparations with VASERETIC.

**Non-steroidal Anti-inflammatory Drugs—**In some patients, the administration of a non-steroidal anti-inflammatory agent can reduce the diuretic, natriuretic, and antihypertensive effects of loop, potassium-sparing and thiazide diuretics. Therefore, when VASERETIC and non-steroidal anti-inflammatory agents are used concomitantly, the patient should be observed closely to determine if the desired effect of the diuretic is obtained.

**Carcinogenesis, Mutagenesis, Impairment of Fertility:** Enalapril in combination with hydrochlorothiazide was not mutagenic in the Ames microbial mutagen test with or without metabolic activation. Enalapril-hydrochlorothiazide did not produce DNA single strand breaks in an *in vitro* alkaline elution assay in rat hepatocytes or chromosomal aberrations in an *in vitro* mouse

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bone marrow assay.

**Enalapril Maleate:** There was no evidence of a tumorigenic effect when enalapril was administered for 106 weeks to rats at doses up to 90 mg/kg/day (150 times\* the maximum daily human dose). Enalapril has also been administered for 94 weeks to male and female mice at doses up to 90 and 180 mg/kg/day, respectively, (150 and 300 times\* the maximum daily dose for humans) and showed no evidence of carcinogenicity.

Neither enalapril maleate nor the active diacid was mutagenic in the Ames microbial mutagen test with or without metabolic activation. Enalapril was also negative in the following genotoxicity studies: reverse mutation assay with *E. coli*, sister chromatid exchange with cultured mammalian cells, and the micronucleus test with mice, as well as in an *in vitro* cytogenetic study using mouse bone marrow.

There were no adverse effects on reproductive performance in male and female rats treated with 10 to 90 mg/kg/day of enalapril.

**Hydrochlorothiazide:** Two-year feeding studies in mice and rats conducted under the auspices of the National Toxicology Program (NTP) uncovered no evidence of a carcinogenic potential of hydrochlorothiazide in female mice (at doses of up to approximately 600 mg/kg/day) or in male and female rats (at doses of up to approximately 100 mg/kg/day). The NTP, however, found equivocal evidence for hepatocarcinogenicity in male mice.

Hydrochlorothiazide was not genotoxic *in vitro* in the Ames mutagenicity assay of *Salmonella typhimurium* strains TA 98, TA 100, TA 1535, TA 1537, and TA 1538 and in the Chinese Hamster Ovary (CHO) test for chromosomal aberrations, or *in vivo* in assays using mouse germinal cell chromosomes, Chinese hamster bone marrow chromosomes, and the *Drosophila* sex-linked recessive lethal trait gene. Positive test results were obtained only in the *in vitro* CHO Sister Chromatid Exchange (dasignogenicity) and in the Mouse Lymphoma Cell (mutagenicity) assays, using concentrations of hydrochlorothiazide from 43 to 1300 µg/mL, and in the *Aspergillus nidulans* non-disjunction assay at an unspecified concentration.

Hydrochlorothiazide had no adverse effects on the fertility of mice and rats of either sex in studies wherein these species were exposed, via their diet, to doses of up to 100 and 4 mg/kg, respectively, prior to conception and throughout gestation.

**Pregnancy:** Pregnancy Categories C (first trimester) and D (second and third trimesters). See WARNINGS, Pregnancy, Enalapril Maleate, Fetal/Neonatal Morbidity and Mortality.

**Nursing Mothers:** Enalapril and enalaprilat are detected in human milk in trace amounts. Thiazides do appear in human milk. Because of the potential for serious reactions in nursing infants from either drug, a decision should be made whether to discontinue nursing or to discontinue VASERETIC, taking into account the importance of the drug to the mother.

**Pediatric Use:** Safety and effectiveness in children have not been established.

**ADVERSE REACTIONS:** VASERETIC has been evaluated for safety in more than 1500 patients, including over 300 patients treated for one year or more. In clinical trials with VASERETIC no adverse experiences peculiar to this combination drug have been observed. Adverse experiences that have occurred, have been limited to those that have been previously reported with enalapril or hydrochlorothiazide.

The most frequent clinical adverse experiences in controlled trials were: dizziness (8.6 percent), headache (5.5 percent), fatigue (3.9 percent) and cough (3.5 percent). Adverse experiences occurring in greater than two percent of patients treated with VASERETIC in controlled clinical trials were: muscle cramps (2.7 percent), nausea (2.4 percent), asthenia (2.4 percent), orthostatic effects (2.3 percent), impotence (2.2 percent), and diarrhea (2.1 percent).

Clinical adverse experiences occurring in 0.5 to 2.0 percent of patients in controlled trials included: *Body As A Whole:* Syncope, chest pain, abdominal pain; *Cardiovascular:* Orthostatic hypotension, palpitation, tachycardia; *Digestive:* Vomiting, dyspepsia, constipation, flatulence, dry mouth; *Nervous/Psychiatric:* Insomnia, nervousness, paresthesia, somnolence, vertigo; *Skin:* Pruritus, rash; *Other:* Dyspnea, gout, back pain, arthralgia, diaphoresis, decreased libido, incontinence, urinary tract infection.

**Angioedema:** Angioedema has been reported in patients receiving VASERETIC (0.6 percent). Angioedema associated with laryngeal edema may be fatal. If angioedema of the face, extremities, lips, tongue, glottis and/or larynx occurs, treatment with VASERETIC should be discontinued and appropriate therapy instituted immediately. (See WARNINGS.)

**Hypotension:** In clinical trials, adverse effects relating to hypotension occurred as follows: hypotension (0.9 percent), orthostatic hypotension (1.5 percent), other orthostatic effects (2.3 percent). In addition syncope occurred in 1.3 percent of patients. (See WARNINGS.)

**Cough:** See PRECAUTIONS, Cough.

**Clinical Laboratory Test Findings; Serum Electrolytes:** See PRECAUTIONS.

**Creatinine, Blood Urea Nitrogen:** In controlled clinical trials minor increases in blood urea nitrogen and serum creatinine, reversible upon discontinuation of therapy, were observed in about 0.6 percent of patients with essential hypertension treated with VASERETIC. More marked increases have been reported in other enalapril experience. Increases are more likely to occur in patients with renal artery stenosis. (See PRECAUTIONS.)

**Serum Uric Acid, Glucose, Magnesium, and Calcium:** See PRECAUTIONS.

**Hemoglobin and Hematocrit:** Small decreases in hemoglobin and hematocrit (mean decreases of approximately 0.3 g percent and 1.0 vol percent, respectively) occur frequently in hypertensive patients treated with VASERETIC but are rarely of clinical importance unless another cause of anemia coexists. In clinical trials, less than 0.1 percent of patients discontinued therapy due to anemia.

**Liver Function Tests:** Rarely, elevations of liver enzymes and/or serum bilirubin have occurred. Other adverse reactions that have been reported with the individual components are listed below and, within each category, are in order of decreasing severity.

**Enalapril Maleate:** Enalapril has been evaluated for safety in more than 10,000 patients. In clinical trials adverse reactions which occurred with enalapril were also seen with VASERETIC. However, since enalapril has been marketed, the following adverse reactions have been reported: *Body As A Whole:* Anaphylactoid reactions (see PRECAUTIONS, Hemodialysis Patients); *Cardiovascular:* Cardiac arrest; myocardial infarction or cerebrovascular accident, possibly secondary to excessive hypotension in high risk patients (see WARNINGS, Hypotension); pulmonary embolism and infarction; pulmonary edema; rhythm disturbances including atrial tachycardia and bradycardia; atrial fibrillation; hypotension; angina pectoris; *Digestive:* Ileus, pancreatitis, hepatic failure, hepatitis (hepatocellular [proven on challenge] or cholestatic jaundice), melena, anorexia, glossitis, stomatitis, dry mouth; *Hematologic:* Rare cases of neutropenia, thrombocytopenia and bone marrow depression. Hemolytic anemia, including cases of hemolysis in patients with G-6-PD deficiency, has been reported, a causal relationship to enalapril has not been established. *Nervous System/Psychiatric:* Depression, confusion, ataxia, peripheral neuropathy (e.g., paresthesia, dyesthesia); *Urogenital:* Renal failure, oliguria, renal dysfunction (see PRECAUTIONS), flank pain, gynecomastia; *Respiratory:* Pulmonary infiltrates, bronchospasm, pneumonia, bronchitis, rhinorrhea, sore throat and hoarseness, asthma, upper respiratory infection; *Skin:* Exfoliative dermatitis, toxic epidermal necrolysis, Stevens-Johnson syndrome, herpes zoster, erythema multiforme, urticaria, pemphigus, alopecia, flushing, photosensitivity; *Special Senses:* Blurred vision, taste alteration, anosmia, conjunctivitis, dry eyes, tearing.

**Miscellaneous:** A symptom complex has been reported which may include a positive ANA, an elevated erythrocyte sedimentation rate, arthralgia/arthritis, myalgia/myositis, fever, serositis, vasculitis, leukocytosis, eosinophilia, photosensitivity, rash and other dermatologic manifestations.

**Fetal/Neonatal Morbidity and Mortality:** See WARNINGS, Pregnancy, Enalapril Maleate, Fetal/Neonatal Morbidity and Mortality.

**Hydrochlorothiazide:** *Body as a Whole:* Weakness; *Digestive:* Pancreatitis, jaundice (intrahepatic cholestatic jaundice), saladenitis, cramping, gastric irritation, anorexia; *Hematologic:* Aplastic anemia, agranulocytosis, leukopenia, hemolytic anemia, thrombocytopenia; *Hypersensitivity:* Purpura, photosensitivity, urticaria, necrotizing angitis (vasculitis and cutaneous vasculitis), fever, respiratory distress including pneumonitis and pulmonary edema, anaphylactic reactions; *Musculoskeletal:* Muscle spasm; *Nervous System/Psychiatric:* Restlessness; *Renal:* Renal failure, renal dysfunction, interstitial nephritis (see WARNINGS); *Skin:* Erythema multiforme including Stevens-Johnson syndrome, exfoliative dermatitis including toxic epidermal necrolysis, alopecia; *Special Senses:* Transient blurred vision, xanthopsia.

\* Based on patient weight of 50 kg.

For more detailed information, consult your DuPont Pharma Representative or see Prescribing Information.

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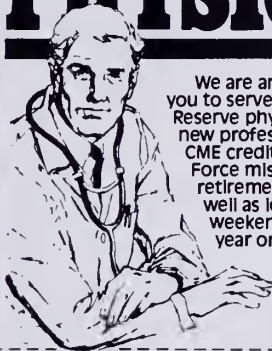


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**CASE RECORDS  
OF THE  
DEPARTMENT OF MEDICINE  
UNIVERSITY OF MISSISSIPPI  
MEDICAL CENTER**

**Clinicopathologic Conference III**

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**Matt Rees, MD**

**Francesco Simeone, MD**

**Joe C. Files, MD, *Editor***

**Differential Diagnosis:** Stanley W. Chapman,  
MD

**Radiological Findings:** Mai Salf, MD

**Pathological Findings:** Nanette Pinkard, MD

**CASE PRESENTATION**

An 84 year old white man was brought to the Veterans Administration Hospital after being found on the floor at home. He apparently had fallen and was unable to get up. The patient was alert and oriented when he was discovered, but he could not recall the events surrounding the fall. He denied loss of consciousness and bowel or bladder incontinence. He did report having chills, generalized weakness and polydipsia for one week prior to admission. He also complained of severe right hip pain and stated that he had a prosthetic right hip placed 15 years earlier for arthritis. He denied any visual disturbance, headaches, diplopia, focal weakness or sensory deficits. The patient's previous medical history was significant for hypertension, sigmoid diverticulosis, iron deficiency anemia, glaucoma, transient ischemic attacks, cerebral vascular accident and pacemaker placement for sick sinus syndrome. His medications on admission were alpha-methyldopa 500 mg once daily, a triamterine/hydrochlorothiazole combination (37.5/25 mg) as a single daily dose, docusate sodium 100 mg twice daily, ferrous sulfate 325 mg thrice daily, and folic acid 1 mg per day.

On physical examination he was a well developed white male in no acute distress. He was alert and fully oriented. His oral temperature was 98.6 F, blood pressure was 140/70, pulse was 88 and he was breathing comfortably at 20 per minute. Examination of the eyes revealed changes compatible with glaucoma bilaterally and a previously described non-reactive enlarged right pupil. The remainder of his head and neck examination was unremarkable except for dry mucous membranes. Lung examination revealed rales at both lung bases and cardiac examination revealed an I/VI apical murmur which did not radiate. Abdominal examination was normal. The patient was noted to hold his right leg abducted and in external rotation. Slight shortening of the leg was also noted, and severe pain was evoked on flexion of his right hip. Arterial pulses in both lower extremities were diminished but equal bilaterally. Neurological examination revealed only decreased sharp and light touch sensation of both lower extremities in a stocking distribution.

Admission laboratory included a white blood cell count of 22,600/mm<sup>3</sup> with 75% segmented neutrophils, 18% band forms, and 6% lymphocytes; the hematocrit was 29.6% and platelet count was 219,000/mm<sup>3</sup>. Serum electrolytes were normal. Serum creatinine was 1.6mg/dl, and BUN was 21 mg/dl. Mild elevations in the liver tests were noted with a total bilirubin of 1.9 mg/dl and SGOT of 53 U/L. The alkaline phosphatase was 73 U/L. Urinalysis was positive for nitrites, with a pH of 5.0 and the specific gravity of 1.029; 5 to 6 white cells per high powered field were visible on microscopic exam. Admission chest radiograph revealed cardiomegaly with increased pulmonary vascularity compatible with congestive heart failure. Radiographs of the pelvis revealed the previous resection of the head and neck of the right femur but no other gross abnormalities. There was normal alignment and positioning of the hip prosthesis.

The day after admission the patient had a temperature elevation to 100.4°F and transient hypotension which resolved after intravenous fluids. Two sets of blood cultures were collected and intravenous ampicillin-sulbactam (1.5 G every six hours) was started. Blood cultures subsequently grew large gram-positive anaerobic rods identified as *Clostridium tertium*. Two diagnostic tests were obtained and a procedure was performed.

**Dr. Chapman** - In summary, this 84 year old gentleman presented with a one week history of chills, a syncopal episode and severe right hip pain.



His past medical history was significant for iron deficiency anemia, sigmoid diverticulosis, atherosclerosis, sick sinus syndrome, cardiac pacemaker and a prosthetic hip. His exam was remarkable only as regards his right lower extremity which was shortened, externally rotated and severely painful with motion. Laboratory studies revealed a modest leukocytosis with left shift, anemia, elevated creatinine and a mild elevation of his total bilirubin and transaminase. *Clostridium tertium* bacteremia was documented after admission. Examination did not reveal a specific focus of infection that is usually associated with clostridial infection such as skin and soft tissue infection, intraabdominal infection, or pleuropulmonary infection. No rectal examination or testing for occult blood on the stool was performed. The presence of occult blood in the stool would be suggestive of a gastrointestinal source of bacteremia, especially in the context of the patient's iron deficiency anemia. The absence of a primary focus of infection suggests that this patient has primary clostridial bacteremia. Other terms used interchangeably in the literature for this syndrome include "benign", "transient" or "non-sustained" clostridial bacteremia. I would first like Dr. Saif to discuss the radiologic findings in this case.

**Dr. Saif:** CT head scan shows a large amount of atrophy and he has a well demarcated area of decreased attenuation most likely consistent with an old blood clot. I did not see an evidence of anything new. This is the admission chest x-ray, as you can see there large heart, the vascularity is increased with some cephalization. This is consistent with CHF. The pelvic x-ray shows a total hip prosthesis with a cement in the acetabulum region. There is no evidence of erosion, cortical break or periosteal elevation. There is no soft tissue swelling that I can see.

**Dr. Chapman:** In organizing my discussion of this case, I have chosen to discuss four basic concepts as regards clostridial infections. First, I will discuss the microbiology of *Clostridia*, with some emphasis on the non-perfringens *Clostridia* as noted in today's case. Next, I will review the various clinical syndromes due to *Clostridia*, including primary clostridial bacteremia, and I will specifically discuss those medical conditions which predispose to blood stream invasion. Finally, I will review the antibiotic therapy and surgical management of *Clostridia* infections. With this background, I will then speculate as to the primary

source of this man's *Clostridium tertium* bacteremia and which diagnostic tests and therapeutic interventions were most likely employed.

*Clostridia* species are gram positive, spore forming, anaerobic rods and are ubiquitous in the environment and in animals.<sup>1</sup> *Clostridia* species have been isolated from soil, decaying vegetation and the intestines of both humans and animals. Soil may contain up to  $10^8$  *Clostridia* per gram, while stool contains up to  $10^9$  organisms per gram. *Clostridia* have also been isolated as part of the normal genital flora in 5 to 10% of women. Clostridial infections are often classified as either endogenous or exogenous. Those infections originating from the patient's own gastrointestinal, cutaneous or vaginal flora have been considered endogenous; most invasive infections due to *Clostridia* are endogenous. Botulism, tetanus, food poisoning and invasive infections resulting from soil contamination of traumatic wounds have been classified as exogenous.

There are over a 100 species of *Clostridia* which are classified by the morphology of the rods, the location of their spores, biochemical reactions and gas liquid chromatography.<sup>1</sup> Despite the large number of species identified, only a relatively few are isolated clinically. The two most common are *C. perfringens* and *C. ramosum* which account for approximately 25% and 15%, respectively, of *Clostridia* species isolated from clinical specimens. Other common isolates include *C. sporogenes* and *C. innocuum*. *Clostridium tertium*, the organism in our case today, is isolated in approximately 3% of clinical specimens.<sup>1,2</sup>

Although *Clostridia* are anaerobic bacteria, their ability to withstand different concentrations of oxygen vary greatly.<sup>1</sup> *Clostridium tertium* is aerotolerant and can survive in the presence of oxygen. It often grows on routine aerobic blood plates and may be misdiagnosed in the laboratory as a *Bacillus* species. Many *Clostridia*, especially the non-perfringens *Clostridia*, are gram-variable and at times appear to be gram-negative in specimens.<sup>1</sup> This can also result in misdiagnosis.

*Clostridia* require a lowered tissue redox potential to produce infection. This environment is produced by tissue necrosis, tissue ischemia due to severe atherosclerosis or tissue around a foreign body. The resulting clinical syndrome is related to exotoxins produced by the organism.<sup>1,2,3</sup> These toxins are divided into three different categories: enterotoxins, neurotoxins, and histotoxins. The enterotoxins cause the gastrointestinal syndromes produced by *Clostridium perfringens* and *Clostridium*

*difficile*. The neurotoxins produced by *C. tetani* and *C. botulinum* cause tetanus and botulism. The histotoxins are capable of destroying cells. Many species, including *C. perfringens*, *C. septicum*, *C. ramosum* and *C. tertium* can produce multiple toxins. Of the 12 lethal toxins that have been identified for *Clostridia*, four are clinically the most important: alpha, beta, epsilon and iota. The alpha toxin, also known as phospholipase c, is the major toxin. It is a lecithinase and is able to attack cell membranes that contain phospholipid and lecithin complexes resulting in cell lysis. This toxin produces necrosis and mediates the hemolysis that is often seen in gas gangrene. This toxin also is a leukotoxin and is responsible for the paucity of white blood cells seen on gram stain of exudates in necrotizing infections caused by *Clostridia*.

*Clostridia* species cause a wide variety of clinical syndromes, most being mediated by toxins. Enteric disease originates within the gut lumen and is mediated by enterotoxins. Examples include food poisoning due to *C. perfringens* and pseudomembranous enterocolitis due to *C. difficile*. Less common enteric syndromes include necrotizing enterocolitis and neutropenic enterocolitis caused by Type C strains of *C. perfringens*. The neurologic syndromes, botulism and tetanus, are due to the toxins produced by *C. botulinum* and *C. tetani*.

A variety of skin and soft tissue infections, both traumatic and non-traumatic, are seen with *Clostridia* species. These include wound colonization, localized abscess, anaerobic cellulitis, suppurative myositis and myonecrosis (gas gangrene). Wounds may be colonized without the organism causing any disease; this is probably the most common finding when *Clostridia* are isolated in clinical specimens. A localized abscess, also referred to as Welch abscess or gas abscess, is also seen and these patients respond well to simple incision and drainage. Anaerobic cellulitis, also known as crepitant cellulitis, is usually a mixed infection. Patients with anaerobic cellulitis have large amounts of air in the soft tissue, but do not have myonecrosis or the fulminant septic course that is seen in patients with clostridial gas gangrene. Infrequently, localized suppurative myositis has been reported, usually in association with intravenous drug use. Clostridial myonecrosis is the most fulminant form of disease and is associated with profound septic shock, severe hemolysis and high mortality.

*Clostridia* also cause a variety of intraabdominal and biliary tract infections, usually

as part of mixed infection. Emphysematous cholecystitis is usually associated with diabetes mellitus, is clinically unique and is identified by large amounts of air in the wall of the gall bladder and throughout the entire biliary system. The radiologic findings are dramatic and easily seen on routine abdominal x-rays. Pulmonary infections associated with *Clostridia* include lung abscess, empyema and mixed necrotizing pneumonia. *Clostridia* may be part of the normal flora of the female genital tract and are associated with pelvic infections in women, including pelvic abscess and tuboovarian abscess. Uterine myonecrosis is a fulminant infection usually seen after a septic abortion and is associated with gas gangrene of the uterus and entire pelvis.

*Clostridia* are uncommon isolates in blood culture, reported in only 1 to 3 % of positive blood cultures.<sup>1,4</sup> *Clostridium perfringens* is isolated most commonly, comprising about 50% of all blood isolates of *Clostridia*. *C. tertium* is seen in only 3% of those blood cultures positive for *Clostridia*. Most bacteremic isolates of *Clostridia* are secondary to the invasive infections already discussed such as intraabdominal infection or skin and soft tissue infection. Primary bacteremia is also reported. In these cases, no obvious focus of infection can be identified as the source of the patient's bacteremia. Other terms utilized in the literature for this syndrome include benign, transient or self-limited clostridial bacteremia. The term benign is frequently used because patients with this syndrome look relatively well. Fever may or may not be present, shock is usually not present and no evidence of hemolysis or myonecrosis is noted. The patient under discussion today demonstrates this syndrome of primary clostridial bacteremia.

Primary clostridial bacteremia is strongly associated with underlying malignancy, especially colorectal cancer and acute leukemia.<sup>4,7</sup> In neutropenic leukemics, autopsy studies have most commonly identify the gastrointestinal tract as the source of bacteremia. Neutropenia in leukemia is associated with a mucositis of the gastrointestinal tract which predisposes to translocation of bacteria across the gut wall, invasion of blood vessels and eventual bacteremia. As evidence of this association, Ingram and colleagues reviewed their 10 year experience involving 26 episodes of clostridial bacteremia in 25 patients.<sup>4</sup> Twenty-two patients had serious underlying diseases and malignancy was seen in approximately half of these. Of patients with cancer, 60% were colorectal. Tanabe et al. reviewed 139 patients with clostridial bacteremia



and cancer.<sup>5</sup> Approximately one-third of these patients had leukemia and one-quarter had colorectal cancers. Bodey and coauthors identified 136 episodes of clostridial bacteremia at the M.D. Anderson Cancer Center over twelve years.<sup>6</sup> The most common underlying malignancies were gastrointestinal, genitourinary carcinomas and acute leukemia. Eighty-three episodes were monomicrobial and 53 episodes were polymicrobial. Mortality was greater in patients with polymicrobial bacteremia (55%) as compared to those patients with monomicrobial clostridial bacteremia (34%). The literature also supports the association of certain non-perfringens *Clostridia* with specific malignancies. *C.septicum*, for example, has been associated with carcinoma of the colon,<sup>8,9</sup> while *C.tertium* is most often associated with leukemia.<sup>10,11,12</sup>

The treatment of clostridial infections includes antibiotics and surgery. For syndromes associated with tissue necrosis and gangrene, whether it be myonecrosis, emphysematous cholecystitis or uterine gangrene, surgery is the critical treatment and antibiotics, although integral to therapy, are secondary. Despite reports of increasing resistance, penicillin is still the drug of choice in the treatment of infections due to *Clostridia*. Doses of penicillin are usually greater than 20 million units per day and given in divided doses every four hours. When present, penicillin resistance in *C.perfringens* is usually mediated by changes in penicillin binding proteins, while resistance in non-perfringens *Clostridia* is mediated by B-lactamase production.<sup>1</sup> This may be relevant to the case presented today in which the patient was treated successfully with a combination of ampicillin and the B-lactamase inhibitor sulbactam. Alternative agents to penicillin include clindamycin, chloramphenicol, metronidazole and imipenem-cilastatin. Reports of resistance to clindamycin in non-perfringens *Clostridia* are increasing. Cephalosporins are not as active against *Clostridia* species when compared to other B-lactams and high levels of resistance to cephalosporins are frequently reported. In particular, *C.tertium* is highly resistant to the cephalosporins and treatment with these agents is identified as a predisposing factor to infection.<sup>10,11,12</sup> *C.tertium* is unusual by also being resistant to penicillin, clindamycin and metronidazole. Interestingly, the organism is susceptible to trimethoprim-sulfamethoxazole, ciprofloxacin and vancomycin. *C.tertium* is reported to be susceptible to combination ampicillin-sulbactam in limited studies.<sup>13</sup>

I would now like to return to the case under discussion. In formulating a diagnostic and thera-

peutic plan, it is essential to first define the primary source of this patient's *C.tertium* bacteremia. In light of his iron-deficiency anemia, the absence of leukemia and the known association of gastrointestinal malignancies with *Clostridia* infections, I believe this patient had a carcinoma of the colon, most likely the cecum. I suspect the lesion perforated, resulting in a pericolic abscess and recurrent clostridial bacteremia. His initial "falling out" was most likely the result of hypotension associated with episodic bacteremia. I believe his hip pain was probably due to septic arthritis caused by bacteremic seeding of the prosthetic hip. Diagnostic tests most helpful in establishing an anatomic diagnosis would be computerized tomography (CT) of the abdomen to identify an abscess and a barium enema to identify an intraluminal defect associated with malignancy. I believe these were the initial diagnostic tests performed and that they confirmed the presence of carcinoma of the colon with an associated intraabdominal abscess. Therapeutic options at this point would include a CT directed drainage of the abscess or a laparotomy for abscess drainage and resection of the cancer. Needle aspiration of the hip was also indicated to rule out septic arthritis. Resection of the prosthesis would be required if septic arthritis was confirmed.

#### Dr. Chapman's Diagnoses:

*Clostridium tertium* bacteremia  
Carcinoma of the cecum  
Intraabdominal abscess  
Septic arthritis of the right hip

#### Dr. Saif: The following are radiology results:

The PA and Lateral Chest x-ray: Comparison with previous films once again reveals marked cardiomegaly, with moderate prominence of the hilar vasculature. Aortic knob calcification is identified. There is diffuse prominence of the interstitial markings, with the presence of Kerley-B lines. A pacing box and wires are identified. The tip appears to project within the right ventricle. No definite evidence of wire disruption is identified. The changes described are consistent with cardiac decompensation and congestive failure. Slightly worse when compared to the previous study.

The pelvis x-ray: Comparison is made with previous studies, and no definite changes can be identified. A total right prosthetic hip device is identified. No evidence of loosening or fracture about this device can be identified. A small amount

of dystrophic calcification is noted within the soft tissues adjacent to the right hip. The visualized bony framework appears somewhat osteopenic without obvious lytic lesions.

**The CT abdomen:** CT slices through the lower abdomen demonstrate increased soft tissue density in the region of the cecum and ascending colon. Contrast within the bowel only partially distends this area and an abnormal soft tissue mass cannot be excluded. CT slices below this level demonstrate a fluid collection with flecks of air consistent with an abscess overlying the right iliac bone medially. This fluid collection appears to extend superiorly, anterior to the psoas muscle and may be related to the abnormal soft tissue mass in the region of the ascending colon described previously. A prosthetic hip is identified on the right. Diffuse vascular calcifications are also noted. A barium enema would be helpful to evaluate the cecal abnormality.

**Barium Enema:** A single contrast barium enema was performed in the usual fashion. This revealed an apple core lesion involving the proximal aspect of the right ascending colon. Numerous small diverticula were identified within the sigmoid colon region. No definite evidence of contrast extravasation could be identified.

**CT Guided Aspiration:** Under CT guidance a #12 French catheter was introduced from an anterior approach into the fluid collection anterior to the right psoas muscle at the level of the iliac vein. A sumpt catheter was introduced into the fluid collection and approximately 20cc of pus was aspirated.

An operative specimen was sent to Pathology. Dr. Pinkard's pathologic report:

**Dr. Pinkard:** Received in pathology was a 17cm length of bowel consisting of a portion of ileum, the cecum, the appendix, a portion of the ascending colon and attached pericolic fat. On opening the bowel, present at the ileocecal valve was a large (6cm in longitudinal axis) circumferential ulcerating lesion with raised borders covered with a thin layer of blood. On sectioning, the tumor appeared to involve the entire wall thickness.

Microscopic examination revealed this lesion to consist of irregular glandular structures composed of cells with hyperchromatic nuclei, occasional nucleoli and an increased nuclear to cytoplasmic ratio. The nuclei were stratified and crowded and few mitoses were present. The surface of the tumor was ulcerated and the neoplastic

glands invaded through the muscularis propria with a surrounding prominent desmoplastic reaction into the pericolic adipose tissue. No vascular invasion was noted and the proximal and distal resection margins were free of tumor.

Six lymph nodes were identified in the adjacent fat and one of the six was replaced by tumor.

At the time of surgery, a frozen section was performed on a suspicious liver lesion. Microscopically this lesion consisted of tumor similar to that present in the colon.

In summary, the final diagnosis was moderately differentiated (grade II) adenocarcinoma of the colon with extension through the musculature into the pericolic fat and metastasis to one of six lymph nodes and the liver. □

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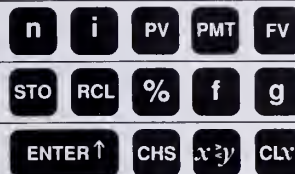
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*Dr. Files is Professor of Medicine and Associate Chairman for Clinical Affairs, Department of Medicine; Dr. Chapman is Professor of Medicine and Dir. Infectious Diseases, Department of Medicine; Dr. Saif, was a Resident, Department of Radiology and Dr. Pinkard, was a Resident, Department of Pathology, all at the University of Mississippi Medical Center.*

*Dr. Adkins, Dr. Rees, and Dr. Simeone were Chief Medicine Residents in the Department of Medicine at the University of Mississippi Medical Center, 1991-92*

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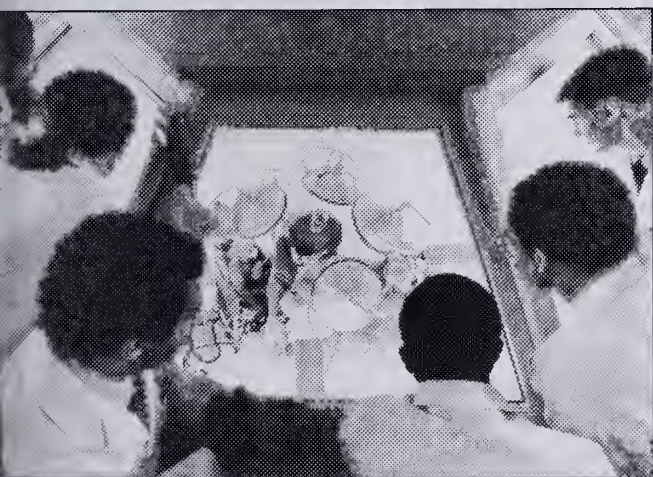
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# Certified Rural Health Clinics Increase Available Health Care

**C**ertified Rural Health Clinics could increase the amount of health care available in certain areas of Mississippi, said David Lightwine, director of MSDH's Office of Rural Health.

Lightwine said changes in federal regulations over the past six years stimulated growth in the number of new clinics applying for certification each year. Mississippi listed eight certified Rural Health Clinics in June 1991, 15 in June 1992, and 37 in June 1993.

"We are delighted to see more providers taking advantage of this program, and we believe that more knowledge and understanding of the program will generate even greater interest," said Lightwine.

Lightwine explained that Congress enacted the Rural Health Clinic Services Act in 1977 as Public Law 95-210. The act authorized cost-based Medicare and Medicaid reimbursement for services provided by mid-level practitioners, such as nurse practitioners and physician assistants, when these services are provided in a certified Rural Health Clinic.

Participation in the program lagged behind initial expectations due to a number of problems associated with the original legislation. To alleviate some of these problems, Congress passed several amendments to the legislation in 1987, 1989, and 1990. The amendments eased the process of certifying a Rural Health Clinic and boosted participation in the program.

Requirements for certification as a Rural Health Clinic include:

(1) Location of the facility in an area defined as rural by the United States Bureau of the Census and designated as a Medically Underserved or Health Professional Shortage Area by the Department of Health and Human Services;

(2) Provision of outpatient primary medical care by mid level practitioners under the general direc-

tion of a physician. In Mississippi, the physician must be located no more than 15 miles from the clinic;

(3) Presence of a certified nurse practitioner at least one-half of the time the clinic is open. This requirement exists even in doctors' offices or hospitals designated as Rural Health Clinics, because the program's goal is to provide health care to more patients than existing physicians in shortage areas would be able to treat;

(4) Compliance with all applicable federal, state, and local requirements and with Medicare and Medicaid health and safety regulations.

Clinics may be provider-based or freestanding. Provider based clinics are part of a hospital, skilled nursing facility, or home health agency. Medicare and Medicaid reimburse provider-based clinics for eligible services according to established cost-reimbursement principles.

"Certification as a Rural Health Clinic may provide a potential new source of income, which is invaluable for small rural hospitals experiencing declines in inpatient revenue. At the same time, these clinics can significantly increase the amount of care available to patients in medically underserved areas," said Lightwine.

For freestanding clinics, Medicare and Medicaid pay a set rate per visit; then adjust the amount to reflect actual costs at the end of the year. The maximum rate allowed per visit is currently \$53.17. Medicare reimburses a clinic 80 percent of the approved rate per visit, with the remainder collected from the patient, while Medicaid reimburses 100 percent.

"This maximum rate is considerably above the reimbursement for a private physician office visit, which serves as an incentive for physicians to establish Rural Health Clinics," Lightwine said. "State



regulations allow physicians to set up satellite clinics as much as 15 miles from their offices, staff these clinics with nurse practitioners supervised by the physician, and receive cost-based reimbursement for the services provided in the satellite clinic. Certification as a Rural Health Clinic helps ensure the financial viability of practices serving large Medicare and Medicaid populations."

Lightwine said one major obstacle to establishing Rural Health Clinics in Mississippi is the shortage of certified nurse practitioners to staff the clinics. Mississippi University for Women offers the only nurse practitioner educational program in Mississippi. Dr. Nancy Hill, director of the program, said the number of inquiries concerning MUW's program doubled from 1992 to 1993. She attributes the increase to soaring demand for nurse practitioners.

"In Mississippi, we could easily place as many graduates as we could possibly train. National figures indicate a need for 5,000 nurse practitioner graduates each year, which is twice the number available," Hill said.

A lack of faculty fuels the shortage both in Mississippi and nationwide. MUW has two vacant faculty positions and needs additional positions. Approximately 76 potential students completed application packets for the 1993-1994 school year. Because of insufficient faculty, the school could accept only 26 of these students. Filling the two vacant positions would allow 12 additional students, Hill said.

Other schools of nursing in the state hope to offer nurse practitioner education in the future. The University of Mississippi Medical Center plans a nurse clinician program beginning in the fall of 1993, which will blend nurse practitioner and clinical nurse specialist competencies with case management skills. Students will work with a selected client group, such as neonates, children, adults, elders, or families; and graduates will be eligible to sit for either nurse practitioner or clinical nurse specialist certification examinations.

Both the MUW and UMC programs award Master of Science in Nursing degrees. The University of Southern Mississippi has requested approval from the Board of Trustees of State Institutions of Higher Learning to begin a Master's degree nurse practitioner program in the fall of 1994.

Lightwine believes increasing the number of nurse practitioner graduates in the state could play a vital role in improving access to health care for people in medically underserved areas, which is the primary goal of the certified Rural Health Clinic



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Owen Brodie, MD, joined CompHealth's locum tenens medical staff in 1989, after 21 years in private practice. Since

then he's worked in temporary assignments in state facilities, filled in for attending physicians, covered for private practitioners across the country.

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program.

"Although every office practice may not benefit from certification as a Rural Health Clinic, we believe the program has great potential advantages," Lightwine said. "The program primarily helps practices with large numbers of Medicare and Medicaid patients, and many areas of Mississippi certainly fall into that category."

"We believe that as more physicians and hospital administrators realize and understand the potential benefits of this program, we will see more and more certified Rural Health Clinics established throughout the state," he said.

For additional information on certified Rural Health Clinics, contact the MSDH Office of Rural Health at (601) 960 7874. For certification materials, contact the MSDH Division of Health Facilities Licensure and Certification at (601) 987-3775.

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## **The President's Page**

**DON Q. MITCHELL, MD**

### **SNOWFLAKES**

"Snowflakes are one of nature's most fragile things, but just look what they can do if they stick together". — Vester M. Kelly

**W**hen I joined my church, they asked for my presence, service, gifts and prayers. The same things could be said about being a part of the medical community. We need your presence at local component society meetings, committee meetings, legislative meetings and the annual session. We need your service both in this association and in the community around us. The public enjoys seeing the positive things that physicians are doing in and for our communities across this state. Many of you are actively involved with your local heart, cancer, or diabetes associations and the list of worthy causes could go on and on. I commend you for this and encourage others to participate.

We need to be cultivating more leaders within our own organization. If this is something you would like to do, please step forward and be counted. The reality of leadership is that it does take time away from your practice, but the results usually benefit the entire medical profession.

As mentioned earlier, the church asked for my gifts. The association occasionally asks for your gifts but for the most part we want you to pay your MSMA dues and encourage others to do so also. It is through dues that this organization is able to work for you. Policies of this association are developed through resolutions presented and discussions held in Reference Committee meetings and voting in the House of Delegates. Each of us has the responsibility inherent with membership to participate in this process. I encourage you to make plans now to attend the January 18, 1994 Legislative Socio-economic Forum and the May 11-15, 1994 MSMA 126th Annual Session.

*(Continued on page 356)*



## "Details, Details"

The most striking impression of the emerging detail of the Clinton health plan is just that, the detail and complexity of an enterprise seeking to reorient a seventh of the American economy. I suppose such complexity was inevitable, given the subject matter, though with twenty-two years in health care I thought I stood at least some chance of understanding it. But confound it, will someone please explain to me just how is the thing going to work? The same question is repeated over and over in hospital corridors, doctors' dressing rooms and during breaks at educational seminars. They wonder how HMOs would work in Mississippi, a state without large metropolitan areas and where the only attempt so far was abandoned. How would global budgets, rationing, that is, be enforced? And who really feels up to dealing with the resulting explosion in demand?

The significance of the fact that the doctors cannot figure this thing out is the assurance that the designers are even more uncertain of what will happen if the plan is ever enacted. For what we are getting here is a glimpse of the catastrophic arrogance that worked tirelessly to exclude from the planning process those whose ideas conflicted with the basic premises of the plan.

A good example of this effect is the concept of enterprise liability, the idea that if a patient feels he has been injured by negligence he can sue only the HMO under which the doctor works, not the doctor himself. Originally the centerpiece of the plan's liability reform, the carrot to the doctors,

the planners were perhaps astonished when the first vehement objections came in from the AMA. Quickly they swept it off the table the way a magician might a card that slipped from his sleeve during an act. They did this ruefully, no doubt, because the only other vegetable they had resembling a carrot was the concept of a single claim form. Yes, there is only a single IRS 1040, but all the attachments to it are perhaps what provoke the open laughter that has been the idea's only reception.

The problem with enterprise liability, of course, is that it destroys the profession of medicine as it has been traditionally known. Doctors have always stood personally responsible to the patient for their work. We have personally answered the phone, personally written prescriptions, and been personally ready to compensate in the case of injury. If the more expensive Ceclor would be a better choice than ampicillin for the patient's illness then in our duty to the patient we prescribed it, often with an explanation why and an apology for having to cause the expense.

Under enterprise liability an HMO could fire a doctor for enough transgressions of that sort. Their tables might show that 90% of respiratory infections clear with drugs old enough to be on a generic formulary, and with an implicit instruction under rationing to use those drugs first, woe to the doctor whose use of Ceclor resulted in litigation over a drug reaction. Doctors in that setting would find working on the patient's behalf extraordinarily difficult.

*(Continued on page 356)*

The editorial opinions expressed in this Journal are those of the indicated author. Editorial opinions are not expressions of the views, or official policies of The Mississippi State Medical Association. We encourage the membership to submit letters for publication regarding any opinion expressed or information contained in the Journal.

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## Editorial

(Continued from page 355)

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This MBAish line of reasoning probably also went through the planner's heads after they withdrew the proposal. What more effective way, they might figure, to cut costs than to destroy the physician's allegiance to the patient? Maybe then these miscreant doctors would pay more careful attention to perfectly valid statistics and tables and quit with their pesky and insistent pointing to exceptions.

Stated another way, enterprise liability is the very blood of this plan. It had to be resurrected and has, if only as "pilot projects" in the 250 page draft proposal released recently to the press. Since we have not been included in the planning we must be ever watchful that such ideas are not slipped into the final print of any law, perhaps in the dark recesses of some conference committee room. It would be all too easy as ideas fly about like arrows, shot by people who just don't understand what they're doing.

**Lee England, MD**  
Associate Editor

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## President's Page

(Continued from page 354)

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With the introduction of the Clinton Administration Health Reform Plan, we, more than ever, need to be a medical community committed to each other. Our association needs to be seen as a positive voice for quality medicine in Mississippi. These things can happen only if you are willing to take the time and make the effort to participate, and encourage others to do the same. As in the snowflake analogy, imagine what we can do if we stick together.

Finally, remember your leadership in your prayers for guidance and decisions that affect our MSMA.

Your Colleague,



## Children Our Future

Through its **Children: Our Future** campaign, the American Academy of Pediatrics aims to put child health at the top of the healthcare reform agenda.

Every child in America deserves a "medical home"—a place to go for regular, comprehensive healthcare. That's important because preventive healthcare is the key to a healthy child.

The nation's pediatricians and the American Academy of Pediatrics are working to improve healthcare for children. As part of the effort, we've declared October as **Child Health Month**. Join us this month as we speak up for children. Help us place solutions before problems.

- **Before it's too late, vaccinate.** Check your records. Immunize your child on time.
- **Give your home a safety check.** Ask your pediatrician about childproofing tips. Most injuries are preventable.
- **Combat substance abuse.** Don't allow smoking around your children. Don't let friends drink and drive.

For a free list of more ways you can help, send a stamped, self-addressed envelope to: *Children Our Future*, Dept. C, American Academy of Pediatrics, P.O. Box 927, Elk Grove Village, IL 60009.

American  
Academy of  
Pediatrics





**Mississippi State Medical  
Association  
125th Annual Session**

**Resolution No. 4**

**Subject:** Increasing Minimum  
Age for Driver's License

**Introduced By:** Central Medical  
Society

**Referred To:** Reference Com-  
mittee on Reports of Officers,  
Board of Trustees and Councils

**Adopted by the Mississippi State  
Medical Association House of  
Delegates on May 2, 1993**

**Whereas,** the Mississippi State  
Medical Association and MSMA  
Auxiliary continue to be deeply  
concerned about the number of in-  
juries and fatalities involving 15-  
19 year old drivers; and

**Whereas,** all Mississippians are  
concerned about the high dropout  
rate in schools of our state; now,  
therefore, be it

**Resolved,** that the Mississippi  
State Medical Association and  
MSMA Auxiliary urge the Gover-  
nor and Mississippi Legislature to  
raise the minimum age for a  
driver's license to age 16, require  
successful completion of the 9th  
grade, or its equivalent, as a pre-  
requisite for initial licensure, and  
provide for a driving permit at age  
15 with a licensed driver age 21  
years or older present in the ve-  
hicle; and be it further

**Resolved,** that the Mississippi  
State Medical Association Presi-  
dent, Board of Trustees, Council  
on Legislation, Council on Public  
Information and state and local  
auxiliaries advise and assist in ef-  
forts to enact these changes.

Most states, years ago, established 16 years of age as the minimum to obtain a drivers license. Mississippi is one of seven states which has a lower age requirement.

Studies by the Insurance Institute for Highway Safety clearly demonstrate the age of the driver is the most important indicator of accident-free driving, more so than any other factor such as driving experience, school grades or drivers education. Statistics from the National Safety Council show that drivers under 16 are over twice as likely to be involved in an auto accident than the general population.

Mississippi physicians specializing particularly in the areas of emergency medicine, pediatrics, and surgery too often see the physical damage that can result from motor vehicle accidents. It is for this reason that a resolution was passed by the MSMA House of Delegates calling for increasing the minimum age to obtain a drivers license in Mississippi.

Motor vehicle crash injuries impose a huge burden on Americans of all ages. The heaviest toll is on our young people. As both drivers and passengers, teenagers are more likely than people of other ages to be involved in motor vehicle crashes. Crash injuries are the leading health problem among 13-19 year olds and are responsible for the deaths of more than 6,000 teenagers every year. Teenage drivers are responsible for a disproportionately high share of crash deaths per license holder, compared to older drivers. And, the majority of fatally injured teenage passengers sustain their injuries in cars driven by other teens.

### **Reasons For Raising the Driving Age to 16**

1. It will save lives and prevent injuries to our children.
2. It will save lives and prevent injuries to others who are involved in auto crashes with 15-year-old drivers.
3. It will save all citizens money by reducing the number of auto accidents in our state.
4. It will save families money as they will not have to purchase auto insurance coverage for their 15-year-old drivers.

What else can be done to reduce the high crash rates of teenage drivers? According to the Insurance Institute for Highway Safety, the policies that are most effective in reducing motor vehicle-related crashes and injuries are those that limit their driving exposure — for example, night and weekend driving curfews. Believe it or not, eliminating high school driver education has been found to reduce teenage crash rates by reducing licensure. Why? High School driver education programs can successfully teach driving skills, and drinking and driving programs can impart knowledge about this behavior. However, attitudes may be unaffected by such programs — and attitudes strongly influence how drivers skills and knowledge are used.

The bottom line is — risk-taking tendencies associated with the immaturity of 15-year-olds are likely to overwhelm the effects of increased skills and knowledge imparted by the education programs. □

## MISSISSIPPI STATE MEDICAL ASSOCIATION

# Membership Benefits

Representation, advocacy, public relations and support of professional ethics are some of the reasons MSMA exists for its members. These are the intangible but important benefits of membership which MSMA seeks to provide through member participation. There are also more tangible benefits which the association provides its members. Illustrated here are the MSMA-sponsored programs for such member needs as insurance and practice management support. These programs are listed below.

### MEMBERSHIP HOTLINE

The MSMA provides a toll free WATS for any member to call to inquire about programs and policies of the association. Inquiries about AMA programs and policies can also be made over a membership WATS line.

### LIAISON SERVICES

MSMA conducts liaison with Travelers Medicare, Medicaid and other third party payor programs on behalf of its members. Individual claim problems, as well as general policy matters, are important aspects of this liaison. For further information call Jackye Wiebelt at MSMA.

### HEALTH INSURANCE

MSMA members who are organized as PAs and wish to provide health insurance coverage for their employees are eligible to participate in a self-insured 501(c)(9) trust sponsored and administered by a subsidiary of the association. For information contact Jackye Wiebelt at MSMA.

### BUSINESS AND PERSONAL INSURANCE

The MS Physicians Insurance Company (MPIC) in cooperation with MSMA offers a wide range of insurance for members of the association. MPIC has a Board of Directors appointed by MSMA composed entirely of practicing physicians who seek to identify the special insurance needs of physicians. For further information contact Jennifer Jones at MPIC.

### PRACTICE MANAGEMENT

Through an arrangement with the AMA Department of Practice Management, MSMA periodically conducts practice management workshops for physician's office personnel. These workshops cover a broad range of topics from CPT-IV coding to patient surveys. For further information call Jackye Wiebelt at MSMA Diversified Services, Inc.

### DEBT COLLECTION SERVICE

Based upon sponsorship by medical associations in many states and its nationwide network, IC System is endorsed by MSMA to perform debt collection services for offices and clinics of member physicians. IC System has a proven track record as a debt collection service. For further information call Robert Kidd at MSMA.

### FINANCIAL/RETIREMENT PLANNING

MSMA members by virtue of their membership in the AMA are eligible to participate in AMA Investment Advisors, Inc. This wholly owned investment subsidiary of the AMA offers a wide range of investment opportunities tailored specifically for physicians. For further information call AMA Advisers.

### MEDICAL MALPRACTICE INSURANCE

The Medical Assurance Company of MS (MACM) was sponsored and organized by MSMA in 1976 to provide a stable market for medical liability insurance to eligible physicians. More than 1500 Mississippi physicians are currently insured by MACM and extensive physician leadership is involved in all phases of MACM's operations. For further information call MACM.

**MSMA and MSMA Diversified Services** - 735 Riverside Drive, Jackson, MS 39202-1166; 601-354-5433 or 800-898-0251 (In-State-WATS).

**AMA Advisers** - 200 N. LaSalle Street, #535, Chicago, IL 60601, 800-525-0864.

**AMA and AMA Membership Hotline** - 515 North State Street, Chicago, IL 60610; 800-AMA-3211.

**Mississippi Physicians Insurance Company** - P.O. Box 5229, Jackson, MS 39296-5229, 601-354-5433 or 800-898-0251 (In-State-WATS).

**Medical Assurance Company of Mississippi** - P.O. Box 4915, Jackson, MS 39296-4915, 601-353-2000 or 800-325-4172 (In -State-WATS).



## MISSISSIPPI STATE MEDICAL ASSOCIATION

# Membership Services

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## **Dr. Webb Chosen Family Physician of the Year by Mississippi Academy**

Dr. Eugene F. Webb, an Itta Bena physician, received the Mississippi Academy of Family Physicians' highest award at the group's recent scientific assembly in Destin, Florida.

The Family Physician of the Year Award is given in recognition of outstanding leadership and services to family medicine in the state. The award was established in honor of the late Dr. John B. Howell, a longtime member and delegate to the American Academy of Family Physicians.

Dr. Webb, an Itta Bena native received two bachelor degrees from the University of Mississippi after junior college and service in the Marine Corps. After intern training a Baptist Hospital in Memphis, Webb returned to Itta Bena to open a family practice in 1955. In 1980, he opened his second office in Greenwood.

He was certified by the American Board of Family Practice in 1972, with his latest recertification in 1990. He is a fellow of the American Academy of Family Physicians and a past president and board member of its Mississippi Chapter.

Dr. Webb is a past president of the Delta Medical Society and past chief of staff and chief of medicine at Greenwood

Leflore Hospital, where he also was chief of the coronary care unit for eight years.

In 1986, Dr. Webb became clinical assistant professor of family medicine at the University of Mississippi Medical Center. He is a member of the Mississippi State Medical Association, the American Medical Association and the Southern Medical Association.

He was chosen outstanding alumnus of the year in 1986 at Mississippi Delta Community college. Dr. Webb is married to the former Mozelle Parker. They are the parents of two children, Jonni Webb, advertising manager of the Northside Sun in Jackson, and Eugene "Jack" Webb Jr, a bank examiner for the Comptroller of Currency. □

## **Thad F. Waites, MD Installed as President of the AHA Mississippi Affiliate.**



Thad F. Waites, MD, of Hattiesburg was recently installed as president of the American Heart Association - Mississippi Affiliate.

Dr. Waites, a cardiologist with Southern Heart Center at the Hattiesburg Clinic, has served on the board of directors and as president-elect of the state organization.

A native of Waynesboro, Dr. Waites received his undergraduate degree from Mississippi College and his medical degree from the University of Mississippi School of Medicine.

Other physicians serving as AHA Mississippi Affiliate officers are: Dr. Clyde O. Hagood, president-elect, of Biloxi; Dr. Joseph Messina, vice-president, of Grenada and Dr. James Hayes, secretary of Jackson. Dr. Thomas J. Herrin, of Jackson has been appointed to the 1993-94 AHA National Nominating and Awards Committee. □



## Carthage Physician Elected President of The MAFP

**Frank W. Bowen, MD** of Carthage was installed as the 45th president of the Mississippi Chapter of the American Academy of Family Physicians (MAFP) at their recent scientific assembly held in Destin, Florida.

Dr. Bowen received his BA and BS from the University of Mississippi and his MD degree from the University of Tennessee. He entered private practice in Walnut Grove, in 1952, moving to Carthage in 1957. He is on staff at the Leake Memorial Hospital; presently serving as chief of staff.

Dr. Bowen is a Charter Fellow of the American Academy of Family Physicians and Charter Diplomat of the American Academy of Family Practice. He has served the MAFP as: program chairman for the scientific assembly, director, secretary/treasurer, vice-president and president-elect.

Dr. William H. Coleman of Scottsboro, Alabama, President-elect of the American Academy of Family Physicians conducted the installation of Dr. Bowen and other MAFP Officers including:

**Dr. Joe D. Herrington** of Natchez, president-elect; **Dr. Edward E. Bryant**, of Kosciusko, vice-president; **Dr. Judy G. Gearhart**, of Clinton, secretary/treasurer; **Dr. Eugene G. Wood, Jr.**, of Jackson, delegate to the AAFP Congress and **Dr. Stanley Hartness** of Kosciusko, Alternate Delegate.

Five physicians were installed as Directors, including: **Dr. David L. Clippinger** of Gulfport; **Dr. David G. Hall** of Natchez; **Dr. Walter G. Gunn** of Quitman; **Dr. Charles F. Brock** of Cleveland; and **Dr. Dwalia S. South** of Ripley.

**Dr. Eugene F. Webb** of Itta Bena received the John B. Howell Memorial Award for Family Doctor of the Year. This award is given yearly to a Family Physician for outstanding leadership and services to family medicine. □

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## Pizza Lunch For 1st and 2nd Year Med Students



*Jim Fuller, a 3rd year Medical Student from Jackson, organized the membership recruitment event and introduced the guest speakers, Drs. Faser Triplett and Don Mitchell.*



MSMA President, Don Q. Mitchell, MD, welcomed 1st and 2nd year medical students to the annual AMA membership recruitment pizza luncheon held in the Nursing Auditorium at UMC. More than 125 students participated.

Organized nationally in 1978, the AMA Medical Student Section has over 33,000 members. The MSS Assembly represents students from 141 accredited US allopathic and osteopathic schools across the country.

Dr. Faser Triplett, of Jackson was guest speaker for the lunch. He spoke to the group about the importance of being involved in organized medicine particularly now in this ever changing practice environment. He also gave them words of encouragement as they began their studies. □



*Pat Scanlon, above, a 4th year medical student from Jackson, signed up 1st and 2nd year students for AMA membership.*

*At right, student members enjoyed an all you can eat pizza lunch.*





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Dr. Elizabeth Keeling is a Board Certified Pediatrician practicing in Jackson, Mississippi.



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## Dr. Pharr Recognized at Goodwill Salute

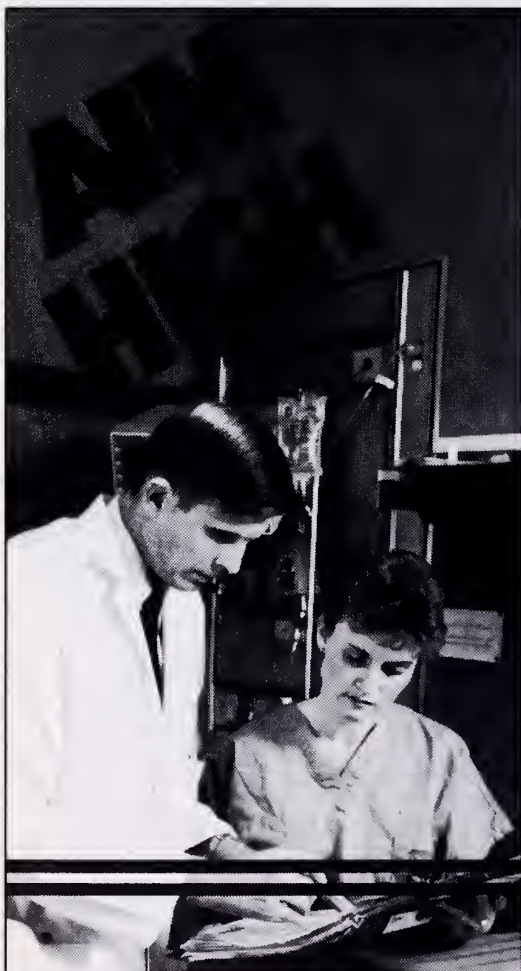
Dr. Max L. Pharr of Jackson was honored recently as an outstanding community volunteer at the Goodwill Industries and Volunteer Services and McRaes Department Stores 1993 Volunteer Salute Luncheon. Dr. Pharr was one of eleven volunteers recognized for their service in the community.

From the onset of his medical career, Dr. Pharr, a family physician has contributed countless hours to community service. Besides being intensely dedicated to patients in his private practice, he has offered volunteer treatment to the children and staff at the Mississippi Methodist Children's Home for 37 years. He has served as the volunteer physician for Friends of Alcoholics and for the Mississippi School for the Blind. He received the Book of Golden Deeds Award from the Oak Forest Exchange Club, was chosen Family Doctor of the Year by the Mississippi Academy of Family Physicians, and was named to the Order of the Golden



*Dr. Max L. Pharr and his wife Betty*

Arrow by Mississippi College — all awards for significant contributions to his community and profession. He has served as president of Central Medical Society, the Mississippi Academy of Family Physicians, and the Mississippi Flying Physicians and as an officer and member of the numerous medical and surgical associations. □



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## Dr. Cobb Honored by Multiple Sclerosis Society

On September 8, 1994, Dr. Alton Cobb was honored at a Multiple Sclerosis Society Dinner of Champions held at the Ramada Coliseum in Jackson.

Friends and family of Dr. Cobb joined together for an evening of fellowship and fund raising.

Jim Malloy, Chairman, Board of Trustees, National Multiple Sclerosis Society Mississippi Chapter, presented Dr. Cobb an award for contributing a lifetime of professional service to the improvement of the health of the people of Mississippi. Dr. Cobb built his career on the belief that the public health system should put its highest priority on prevention and protective health services and that all people should have access to primary health care.

Following dinner, Dr. Cobb and the audience had the opportunity to enjoy the comments and stories told during the "Roast". T. W. Williamson, Kaye W. Bender, and Sam Cameron, all friends and co-workers of Dr. Cobb, took the floor first to tell of their experiences while working with Dr. Cobb. Before the

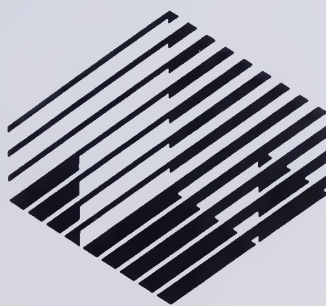
evening was over, Dr. Cobb took the opportunity to respond to his roasters and comment, as you would expect, about the "health of the people of Mississippi". □

## AAP Chapter Receives Recognition

The Mississippi Chapter of the American Academy of Pediatrics was recently named "Outstanding Small Chapter" by the American Academy of Pediatrics. Dr. Susan Buttross, UMC assistant Professor of pediatrics, serves as president of the Chapter. □

### CORRECTION

In the September Issue of the *Journal MSMA*, on page 318, Dr. Susan Buttross's name was omitted as author of the article entitled, "The Mississippi Children's Immunization Awareness Project".



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# The University of Mississippi Medical Center



## UMC Barnard Professors

The six University of Mississippi Medical Center faculty members named Barnard Distinguished Professors for significant scholarly contributions to their disciplines were **Dr. John C. Morrison**, professor and vice-chairman of ob-gyn (seated, left); **Dr. D. Jeanette Pullen**, professor of pediatrics and director of pediatric hematology-oncology (seated, center); **Dr. John E. Hall**, professor and chairman of

physiology and biophysics (seated, right); **Dr. Ing K. Ho**, professor and chairman of pharmacology and toxicology (standing, left center); **Dr. John H. Hembree**, professor and acting chairman of restorative dentistry (standing, center); and **Dr. L. William Clem**, professor and chairman of microbiology (standing right center). Ole Miss Chancellor **R. Gerald Turner** (standing left) and **Dr. Norman C.**

**Nelson**, UMC vice-chancellor for health affairs (standing right), presented the Barnard Professorships. Six Ole Miss faculty members were also named Barnard Professors. Each of the twelve honorees will receive \$10,000 annually for five years. Up to half of the award can be used as a salary supplement with the remainder to be used for research and professional development expenses. □

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Yohimbine exerts a stimulating action on the mood and may increase anxiety. Such actions have not been adequately studied or related to dosage although they appear to require high doses of the drug. Yohimbine has a mild anti-diuretic action, probably via stimulation of hypothalamic centers and release of posterior pituitary hormone.

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**Indications:** Yocon<sup>®</sup> is indicated as a sympatholytic and mydriatic. It may have activity as an aphrodisiac.

**Contraindications:** Renal diseases, and patient's sensitive to the drug. In view of the limited and inadequate information at hand, no precise tabulation can be offered of additional contraindications.

**Warning:** Generally, this drug is not proposed for use in females and certainly must not be used during pregnancy. Neither is this drug proposed for use in pediatric, geriatric or cardio-renal patients with gastric or duodenal ulcer history. Nor should it be used in conjunction with mood-modifying drugs such as antidepressants, or in psychiatric patients in general.

**Adverse Reactions:** Yohimbine readily penetrates the (CNS) and produces a complex pattern of responses in lower doses than required to produce peripheral a-adrenergic blockade. These include, anti-diuresis, a general picture of central excitation including elevation of blood pressure and heart rate, increased motor activity, irritability and tremor. Sweating, nausea and vomiting are common after parenteral administration of the drug.<sup>1,2</sup> Also dizziness, headache, skin flushing reported when used orally.<sup>1,3</sup>

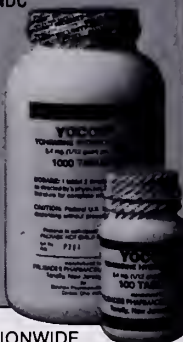
**Dosage and Administration:** Experimental dosage reported in treatment of erectile impotence.<sup>1,3,4</sup> 1 tablet (5.4 mg) 3 times a day, to adult males taken orally. Occasional side effects reported with this dosage are nausea, dizziness or nervousness. In the event of side effects dosage to be reduced to 1/2 tablet 3 times a day, followed by gradual increases to 1 tablet 3 times a day. Reported therapy not more than 10 weeks.<sup>3</sup>

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#### References:

1. A. Morales et al., New England Journal of Medicine: 1221, November 12, 1981.
2. Goodman, Gilman — The Pharmacological basis of Therapeutics 6th ed., p. 176-188. McMillan December Rev. 1/85.
3. Weekly Urological Clinical letter, 27:2, July 4, 1983.
4. A. Morales et al., The Journal of Urology 128: 45-47, 1982.

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## Dr. Robertson Named Director of Continuing Health Professional Education.

Dr. Roland B. Robertson has been named director of continuing health professional education at the University of Mississippi Medical Center.

Dr. Norman C. Nelson, vice chancellor for health affairs announced Dr. Robertson's appointment following approval by the Board of Trustees of State Institutions of Higher Learning.



"He brings an extensive background and excellent credentials to this position," Dr. Nelson said. "We are pleased that he has decided to assume this most important responsibility."

Dr. Robertson joined the UMC School of Medicine faculty as assistant professor in 1969. In 1974, he was appointed first director of the UMC continuing education division, a position he held until 1976 when he was named chief of staff at the Department of Veteran Affairs Medical Center and vice chancellor for VA Affairs.

Dr. Robertson earned the BS in 1955 at the University of Southern Mississippi and the MD in 1958 at the University of Tennessee Medical School. He completed residency training at UMC.

He is a member of the Central Medical Society, Mississippi State Medical Association, Jackson Academy of Medicine, Association of Military Surgeons, American College of Physicians, American Thoracic Society and the Mississippi Thoracic Society, which he served as president from 1971-1972.

A fellow of the American College of Chest Physicians, Dr. Robertson has been State Air Surgeon for the Mississippi Air National Guard since 1989.

□



**J. Patrick Barrett of Jackson**, recently attended the Tenth Annual Meeting of the Southern Orthopaedic Association held in Vienna, Austria.

**Nathan F. Bradford** has associated with The Greenville Clinic, PA for the practice of internal medicine and pediatrics, 1421 E. Union Street, Greenville, MS.

**Alton Cobb**, of Jackson has been recently elected to the board of directors of the Central Mississippi Chapter of the American Red Cross.

**Gary D. Carr**, of Hattiesburg has associated with Sassafras Hill Counseling Center, Inc. as Medical Director of the outpatient program, 4824 Old Highway Eleven, Purvis.

**Jeffery R. Chain** announces the opening of his practice of orthopaedic surgery, sports medicine & joint reconstruction, 307 Hospital Road, Starkville.

**John C. Clay**, of Meridian was elected 1993-94 president-elect of the Southern Association for Oncology.

**Pacita R. Coss** has associated with the Wiggins Clinic in the practice of family medicine, 303 First Street, Wiggins.

**Kari Hatten**, a nephrologist from Jackson, has moved to Clarksdale and joined the Medical Staff of NWRMC. He will continue to manage patients at the Clarksdale Kidney Care Unit in addition to serving hospitalized patients.

**William C. Hopper, Jr.**, of Gulfport, recently attended the Tenth Annual Meeting of the Southern Orthopaedic Association held in Vienna, Austria.

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**Edgar W. Hull**, of Pascagoula recently received a three-year appointment as Cancer Liaison Physician for the Hospital Cancer Program at Singing River Hospital.

**Adron Keith Lay** of Bay Springs has completed continuing medical education requirements to retain active membership in the American Academy of Family Physicians (AAFP).

**Larry R. Lipscomb** announces the relocation of his practice of

obstetrics and gynecology to 1044 North Flowood Drive, Jackson.

**Nelson K. Little** of Oxford was recently inducted into the American College of Cardiology.

**Sherry A. Martin** announces the relocation of her practice of internal medicine to 806 Garfield Street, Tupelo.

**Patrick G. McLain** announces the opening of his medical clinic, Seven Lakeland Circle, Suite, 100, Jackson.

**Hernando Cartes Payne** of Greenville has completed continuing

medical education requirements to retain active membership in the American Academy of Family Physicians.

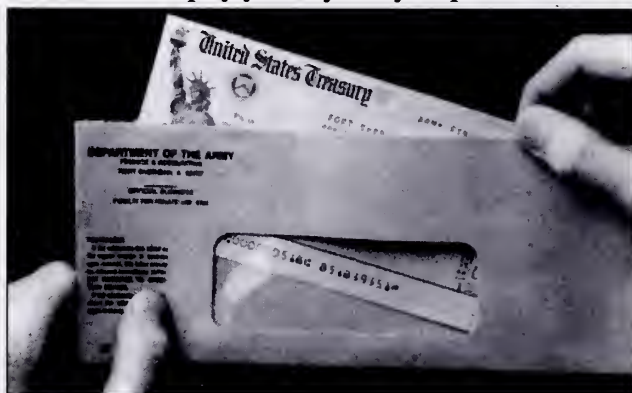
**Steve Senter** and **Jack Senter** announce the opening of the Golden Family Medical Clinic, 74 Red Bay Road, Golden, MS.

**Eugene E. Taylor** of Natchez, has been chosen president of the Southern Orthopaedic Association for 1993-94.

**Horton G. Taylor, Jr.** of Ripley has completed continuing medical education requirements to retain active membership in the American Academy of Family

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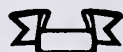
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# Physicians' Recognition Award



Twenty-four MSMA members were named recipients of the AMA Physicians Recognition Award in August 1993. This award is presented by the American Medical Association to Physicians who have voluntarily completed a specified number of continuing medical education hours. These individuals are presented below by Medical Society.

## **CENTRAL MEDICAL SOCIETY**

**Ralph H. Didlake, MD**  
**Donald Grillo, MD**  
**William A. Long, Jr., MD**  
**James N. Martin, Jr., MD**  
**Glen F. Morris, MD**  
**Paul E. Sheffield, MD**  
**David R. Tapley, MD**

## **CLARKSDALE & SIX COUNTIES**

**MEDICAL SOCIETY**  
**Richard E. Waller, MD**

## **COAST COUNTIES MEDICAL SOCIETY**

**Thomas E. Benefield, MD**  
**Craig Martin Slater, MD**

## **DELTA MEDICAL SOCIETY**

**Hernando Cartes Payne, MD**

## **NORTH CENTRAL MEDICAL SOCIETY**

**Thomas P. McGee, Jr., MD**

## **NORTHEAST MISSISSIPPI MEDICAL SOCIETY**

**George Leonard McCain, Jr., MD**  
**John R. Mitchell, MD**

## **NORTH MISSISSIPPI MEDICAL SOCIETY**

**Robert F. Cooper, III, MD**  
**Pravin P. Patel, MD**  
**Horton G. Taylor, MD**

## **PRAIRIE MEDICAL SOCIETY**

**William M. Gillespie, III, MD**  
**G. Leroy Howell, MD**

## **SOUTH CENTRAL MISSISSIPPI MEDICAL SOCIETY**

**Terry E. Westbrook, MD**

## **SOUTH MISSISSIPPI MEDICAL SOCIETY**

**Jacks C. Evans, MD**  
**Richard A. Johnson, MD**  
**J. Bruce Pruett, MD**

## **SINGING RIVER MEDICAL SOCIETY**

**Paul M. Allen, MD**

Applications for the AMA Physicians Recognition award can be obtained at any time by writing or calling the AMA Office of Physician Credentials and Qualifications: (312) 464-4672.



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**Personals/continued**

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Board Certified through the year 2000.

**T. Gregory Terral** has associated with Capital Orthopaedic Clinic, P.A. in the practice of orthopaedic surgery, 971 Lakeland Drive, Suite 315, Jackson.

**Guy T. Vlase, Jr.**, of Jackson, presented a scientific research paper entitled *Design Rationale For A New Cementless Total Hip Prosthesis*, during the Tenth Annual Meeting of the Southern Orthopaedic Association held in Vienna, Austria.

**James C. Waites** of Laurel, recently served as moderator for the symposium *Update on Fam-*

*ily Medicine* sponsored by the Southern Medical Association in conjunction with the Southern Association for Family Practice.

**Prentice Walker** has associated with the Urgent Care Center in the practice of family medicine, Highway 49 South, Hattiesburg.

**Clark G. Warden** of Pascagoula has been elected to membership in the Society of American Gastrointestinal Endoscopic Surgeons.

**Lisa K. Washburn** has associated with **Charles S. Knight, Mitzi Ferguson** and **David F. Wender**, for the practice of neonatal-perinatal medicine, at Woman's Hospital, 1026 North Flowood Drive, Jackson.

**Willie Lee Wells**, of Bruce has

been granted membership in the Southern Medical Association.

**Timothy L. Wright** of Oxford was recently inducted into the American College of Cardiology.

**Walter W. Woody** has associated with Internal Medicine Associates Of Tupelo, Ltd. for the practice of cardiology, 845 South Madison Street, Tupelo. □

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## Index to Advertisers

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Pravachol ..... **third and fourth covers**

CompHealth ..... 353

Disability Determination ..... 375  
Doctors Insurance Reciprocal ..... 371  
Dupont Pharmaceuticals - Vaseretic  
Insert ..... 344 A-B, 345

Medical Assurance Co. of MS ..... 363  
Medley and Company ..... 351  
Mississippi Methodist Rehabilitation  
Center ..... **second cover**  
MS Emergency Association ..... 375  
MS Physicians Insurance Company ..... 8  
MSMA Benefit Plan & Trust ..... 344

Palisades Pharmaceuticals - Yocon ..... 368  
Premier Printing ..... 345

Southern Research Group ..... 361  
St. Dominic/Jackson Memorial Hospital ..... 366

The Doctors' Company ..... 4  
The Sterling Group ..... 343  
Trustmark ..... 365

US Air Force ..... 364  
US Air Force Reserve ..... 345  
US Army Active ..... 351  
US Army Reserve ..... 370



**Reference:** 1. Jones PH, et al. Once-daily pravastatin in patients with primary hypercholesterolemia: a dose-response study. *Clin Cardiol*. 1991;14:146-151.

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### WARNINGS

**Liver Enzymes:** HMG-CoA reductase inhibitors, like some other lipid-lowering therapies, have been associated with biochemical abnormalities of liver function. Increases of serum transaminase (ALT, AST) values to more than 3 times the upper limit of normal occurring on 2 or more (not necessarily sequential) occasions have been reported in 1.3% of patients treated with pravastatin in the U.S. over an average period of 18 months. These abnormalities were not associated with cholestasis and did not appear to be related to treatment duration. In those patients in whom these abnormalities were believed to be related to pravastatin and who were discontinued from therapy, the transaminase levels usually fell slowly to pretreatment levels. These biochemical findings are usually asymptomatic although worldwide experience indicates that anorexia, weakness, and/or abdominal pain may also be present in rare patients.

As with other lipid-lowering agents, liver function tests should be performed during therapy with pravastatin. Serum aminotransferases, including ALT (SGPT), should be monitored before treatment begins, every six weeks for the first three months, every eight weeks during the remainder of the first year, and periodically thereafter (e.g., at about six-month intervals). Special attention should be given to patients who develop increased transaminase levels. Liver function tests should be repeated to confirm an elevation and subsequently monitored at more frequent intervals. If increases in AST and ALT equal or exceed three times the upper limit of normal and persist, then therapy should be discontinued. Persistence of significant aminotransferase elevations following discontinuation of therapy may warrant consideration of liver biopsy.

Active liver disease or unexplained transaminase elevations are contraindications to the use of pravastatin (see CONTRAINDICATIONS). Caution should be exercised when pravastatin is administered to patients with a history of liver disease or heavy alcohol ingestion (see CLINICAL PHARMACOLOGY: Pharmacokinetics/Metabolism). Such patients should be closely monitored, started at the lower end of the recommended dosing range, and titrated to the desired therapeutic effect.

**Skeletal Muscle: Rhabdomyolysis with renal dysfunction secondary to myoglobinuria has been reported with pravastatin and other drugs in this class.** Uncomplicated myalgia has also been reported in pravastatin-treated patients (see ADVERSE REACTIONS). Myopathy, defined as muscle aching or muscle weakness in conjunction with increases in creatine phosphokinase (CPK) values to greater than 10 times the upper limit of normal was reported to be possibly due to pravastatin in only one patient in clinical trials (<0.1%). Myopathy should be considered in any patient with diffuse myalgias, muscle tenderness or weakness, and/or marked elevation of CPK. Patients should be advised to report promptly unexplained muscle pain, tenderness or weakness, particularly if accompanied by malaise or fever. **Pravastatin therapy should be discontinued if markedly elevated CPK levels occur or myopathy is diagnosed or suspected.** Pravastatin therapy should also be temporarily withheld in any patient experiencing an acute or serious condition predisposing to the development of renal failure secondary to rhabdomyolysis, e.g., sepsis; hypotension; major surgery; trauma; severe metabolic, endocrine, or electrolyte disorders; or uncontrolled epilepsy.

The risk of myopathy during treatment with lovastatin is increased if therapy with either cyclosporine, gemfibrozil, erythromycin, or niacin is administered concurrently. There is no experience with the use of pravastatin together with cyclosporine. Myopathy has not been observed in clinical trials involving small numbers of patients who were treated with pravastatin together with niacin. One trial of limited size involving combined therapy with pravastatin and gemfibrozil showed a trend toward more frequent CPK elevations and patient withdrawals due to musculoskeletal symptoms in the group receiving combined treatment as compared with the groups receiving placebo, gemfibrozil, or pravastatin monotherapy. Myopathy was not reported in this trial (see PRECAUTIONS: Drug Interactions). One patient developed myopathy when clofibrate was added to a previously well tolerated regimen of pravastatin; the myopathy resolved when clofibrate therapy was stopped and pravastatin treatment continued. **The use of fibrates alone may occasionally be associated with myopathy. The combined use of pravastatin and fibrates should generally be avoided.**

### PRECAUTIONS

**General:** Pravastatin may elevate creatine phosphokinase and transaminase levels (see ADVERSE REACTIONS). This should be considered in the differential diagnosis of chest pain in a patient on therapy with pravastatin.

**Homozygous Familial Hypercholesterolemia.** Pravastatin has not been evaluated in patients with rare homozygous familial hypercholesterolemia. In this group of patients, it has been reported that HMG-CoA reductase inhibitors are less effective because the patients lack functional LDL receptors.

**Renal Insufficiency:** A single 20 mg oral dose of pravastatin was administered to 24 patients with varying degrees of renal impairment (as determined by creatinine clearance). No effect was observed on the pharmacokinetics of pravastatin or its 3 $\alpha$ -hydroxy isomeric metabolite (SO 31,906). A small increase was seen in mean AUC values and half-life (t<sub>1/2</sub>) for the inactive enzymatic ring hydroxylation metabolite (SO 31,945). Given this small sample size, the dosage administered, and the degree of individual variability, patients with renal impairment who are receiving pravastatin should be closely monitored.

**Information for Patients:** Patients should be advised to report promptly unexplained muscle pain, tenderness or weakness, particularly if accompanied by malaise or fever.

**Drug Interactions:** Immunosuppressive Drugs, Gemfibrozil, Niacin (Nicotinic Acid), Erythromycin. See WARNINGS: Skeletal Muscle.

**Antipyrine:** Clearance by the cytochrome P450 system was unaltered by concomitant administration of pravastatin. Since pravastatin does not appear to induce hepatic drug-metabolizing enzymes, it is not expected that any significant interaction of pravastatin with other drugs (e.g., phenytoin, quinidine) metabolized by the cytochrome P450 system will occur.

**Cholestyramine/Colestipol:** Concomitant administration resulted in an approximately 40 to 50% decrease in the mean AUC of pravastatin. However, when pravastatin was administered 1 hour before or 4 hours after cholestyramine or 1 hour before colestipol and a standard meal, there was no clinically significant decrease in bioavailability or therapeutic effect. (See DOSAGE AND ADMINISTRATION: Concomitant Therapy.)

**Warfarin:** In a study involving 10 healthy male subjects given pravastatin and warfarin concomitantly for 6 days, bioavailability parameters at steady state for pravastatin (parent compound) were not altered. Pravastatin did not alter the plasma protein-binding of warfarin. Concomitant dosing did increase the AUC and C<sub>max</sub> of warfarin but did not produce any changes in its anticoagulant action (i.e., no increase was seen in mean prothrombin time after 6 days of concomitant therapy). However, bleeding and extreme prolongation of prothrombin time has been reported with another drug in this class. Patients receiving warfarin-type anticoagulants should have their prothrombin times closely monitored when pravastatin is initiated or the dosage of pravastatin is changed.

**Cimetidine:** The AUC<sub>0-12h</sub> for pravastatin when given with cimetidine was not significantly different from the AUC for pravastatin when given alone. A significant difference was observed between the AUC's for pravastatin when given with cimetidine compared to when administered with antacid.

**Digoxin:** In a crossover trial involving 18 healthy male subjects given pravastatin and digoxin concurrently for 9 days, the bioavailability parameters of digoxin were not affected. The AUC of pravastatin tended to increase, but the overall bioavailability of pravastatin plus its metabolites SO 31,906 and SO 31,945 was not altered.

**Gemfibrozil:** In a crossover study in 20 healthy male volunteers given concomitant single doses of pravastatin and gemfibrozil, there was a significant decrease in urinary excretion and protein binding of pravastatin. In addition, there was a significant increase in AUC, C<sub>max</sub>, and T<sub>max</sub> for the pravastatin metabolite SO 31,906. Combination therapy with pravastatin and gemfibrozil is generally not recommended.

In interaction studies with aspirin, antacids [1 hour prior to PRAVACHOL (pravastatin sodium)], cimetidine, nicotinic acid, or probucol, no statistically significant differences in bioavailability were seen when PRAVACHOL was administered.

**Other Drugs:** During clinical trials, no noticeable drug interactions were reported when PRAVACHOL was added to: diuretics, antihypertensives, digitalis, converting-enzyme inhibitors, calcium channel blockers, beta-blockers, or nitroglycerin.

**Endocrine Function:** HMG-CoA reductase inhibitors interfere with cholesterol synthesis and lower circulating cholesterol levels and, as such, might theoretically blunt adrenal or gonadal steroid hormone production. Results of clinical trials with pravastatin in males and post-menopausal females were inconsistent with regard to possible effects of the drug on basal steroid hormone levels. In a study of 21 males, the mean testosterone response to human chorionic gonadotropin was significantly reduced (p<0.004) after 16 weeks of treatment with 40 mg of pravastatin. However, the percentage of patients showing a  $\geq$ 50% rise in plasma testosterone after human chorionic gonadotropin stimulation did not change significantly after therapy in these patients. The effects of HMG-CoA reductase inhibitors on spermatogenesis and fertility have not been studied in adequate numbers of patients. The effects, if any, of pravastatin on the pituitary-gonadal axis in pre-menopausal females are unknown. Patients treated with pravastatin who display clinical evidence of endocrine dysfunction should be evaluated appropriately. Caution should also be exercised if an HMG-CoA reductase inhibitor or other agent used to lower cholesterol levels is administered to patients also receiving other drugs (e.g., ketoconazole, spironolactone, cimetidine) that may diminish the levels or activity of steroid hormones.

**CNS Toxicity:** CNS vascular lesions, characterized by perivascular hemorrhage and edema and mononuclear cell

infiltration of perivascular spaces, were seen in dogs treated with pravastatin at a dose of 25 mg/kg/day, a dose that produced a plasma drug level about 50 times higher than the mean drug level in humans taking 40 mg/day. Similar CNS vascular lesions have been observed with several other drugs in this class.

A chemically similar drug in this class produced optic nerve degeneration (Wallerian degeneration of retinoganglionic fibers) in clinically normal dogs in a dose-dependent fashion starting at 60 mg/kg/day, a dose that produced mean plasma drug levels about 30 times higher than the mean drug level in humans taking the highest recommended dose (as measured by total enzyme inhibitory activity). This same drug also produced vestibulocochlear (Wallerian-like) degeneration and retinal ganglion cell chromatolysis in dogs treated for 14 weeks at 180 mg/kg/day, a dose which resulted in a mean plasma drug level similar to that seen with the 60 mg/kg dose.

**Carcinogenesis, Mutagenesis, Impairment of Fertility:** In a 2-year study in rats fed pravastatin at doses of 10, 30, or 100 mg/kg body weight, there was an increased incidence of hepatocellular carcinomas in males at the highest dose (p<0.01). Although rats were given up to 125 times the human dose (HD) on a mg/kg body weight basis, their serum drug levels were only 6 to 10 times higher than those measured in humans given 40 mg pravastatin as measured by AUC.

The oral administration of 10, 30, or 100 mg/kg (producing plasma drug levels approximately 0.5 to 5.0 times human drug levels at 40 mg) of pravastatin to mice for 22 months resulted in a statistically significant increase in the incidence of malignant lymphomas in treated females when all treatment groups were pooled and compared to controls (p<0.05). The incidence was not dose-related and male mice were not affected.

A chemically similar drug in this class was administered to mice for 72 weeks at 25, 100, and 400 mg/kg body weight, which resulted in mean serum drug levels approximately 3, 15, and 33 times higher than the mean human serum drug concentration (as total inhibitory activity) after a 40 mg oral dose. Liver carcinomas were significantly increased in high-dose females and mid- and high-dose males, with a maximum incidence of 90 percent in males. The incidence of adenomas of the liver was significantly increased in mid- and high-dose females. Drug treatment also significantly increased the incidence of lung adenomas in mid- and high-dose males and females. Adenomas of the eye Harderian gland (a gland of the eye of rodents) were significantly higher in high-dose mice than in controls.

No evidence of mutagenicity was observed *in vitro*, with or without rat-liver metabolic activation, in the following studies: microbial mutagen tests, using mutant strains of *Salmonella typhimurium* or *Escherichia coli*, a forward mutation assay in L5178Y TK +/– mouse lymphoma cells; a chromosomal aberration test in hamster cells, and a gene conversion assay using *Saccharomyces cerevisiae*. In addition, there was no evidence of mutagenicity in either a dominant lethal test in mice or a micronucleus test in mice.

In a study in rats, with daily doses up to 500 mg/kg, pravastatin did not produce any adverse effects on fertility or general reproductive performance. However, in a study with another HMG-CoA reductase inhibitor, there was decreased fertility in male rats treated for 34 weeks at 25 mg/kg body weight, although this effect was not observed in a subsequent fertility study when the same dose was administered for 11 weeks (the entire cycle of spermatogenesis, including epididymal maturation). In rats treated with this same reductase inhibitor at 180 mg/kg/day, seminiferous tubule degeneration (necrosis and loss of spermatogenic epithelium) was observed. Although not seen with pravastatin, two similar drugs in this class caused drug-related testicular atrophy, decreased spermatogenesis, spermatocytic degeneration, and giant cell formation in dogs. The clinical significance of these findings is unclear.

**Pregnancy: Pregnancy Category X:** See CONTRAINDICATIONS.

Safety in pregnant women has not been established. Pravastatin was not teratogenic in rats at doses up to 1000 mg/kg daily or in rabbits at doses of up to 50 mg/kg daily. These doses resulted in 20x (rabbit) or 240x (rat) the human exposure based on surface area (mg/m<sup>2</sup>). However, in studies with another HMG-CoA reductase inhibitor, skeletal malformations were observed in rats and mice. PRAVACHOL (pravastatin sodium) should be administered to women of child-bearing potential only when such patients are highly unlikely to conceive and have been informed of the potential hazards. If the woman becomes pregnant while taking PRAVACHOL, it should be discontinued and the patient advised again as to the potential hazards to the fetus.

**Nursing Mothers:** A small amount of pravastatin is excreted in human breast milk. Because of the potential for serious adverse reactions in nursing infants, women taking PRAVACHOL should not nurse (see CONTRAINDICATIONS).

**Pediatric Use:** Safety and effectiveness in individuals less than 18 years old have not been established. Hence, treatment in patients less than 18 years old is not recommended at this time. (See also PRECAUTIONS: General.)

### ADVERSE REACTIONS

Pravastatin is generally well tolerated, adverse reactions have usually been mild and transient. In 4-month long placebo-controlled trials, 1.7% of pravastatin-treated patients and 1.2% of placebo-treated patients were discontinued from treatment because of adverse experiences attributed to study drug therapy, this difference was not statistically significant. In long-term studies, the most common reasons for discontinuation were asymptomatic serum transaminase increases and mild, non-specific gastrointestinal complaints. During clinical trials the overall incidence of adverse events in the elderly was not different from the incidence observed in younger patients.

**Adverse Clinical Events:** All adverse clinical events (regardless of attribution) reported in more than 2% of pravastatin-treated patients in the placebo-controlled trials are identified in the table below; also shown are the percentages of patients in whom these medical events were believed to be related or possibly related to the drug:

Body System/Event	All Events %		Events Attributed to Study Drug %	
	Pravastatin (N = 900)	Placebo (N = 411)	Pravastatin (N = 900)	Placebo (N = 411)
Cardiovascular				
Cardiac Chest Pain	4.0	3.4	0.1	0.0
Dermatologic				
Rash	4.0*	1.1	1.3	0.9
Gastrointestinal				
Nausea/Vomiting	7.3	7.1	2.9	3.4
Diarrhea	6.2	5.6	2.0	1.9
Abdominal Pain	5.4	6.9	2.0	3.9
Constipation	4.0	2.4	2.4	5.1
Flatulence	3.3	2.4	3.4	3.4
Heartburn	2.9	1.9	0.7	0.7
General				
Fatigue	3.8	3.4	1.9	1.0
Chest Pain	3.7	3.0	0.3	0.2
Influenza	2.4*	0.0	0.0	0.0
Musculoskeletal				
Localized Pain	10.0	9.0	4.4	1.5
Myalgia	2.7	1.0	0.6	0.0
Nervous System				
Headache	6.2	5.6	1.7*	0.2
Dizziness	3.3	3.2	1.0	0.5
Renal/Genitourinary				
Urinary Abnormality	2.4	2.9	0.7	1.2
Respiratory				
Common Cold	7.0	6.3	0.0	0.0
Rhinitis	4.0	4.1	0.1	0.0
Cough	2.6	1.7	0.1	0.0

\*Statistically significantly different from placebo.

The following effects have been reported with drugs in this class:

**Skeletal:** myopathy, rhabdomyolysis.

**Neurological:** dysfunction of certain cranial nerves (including alteration of taste, impairment of extra-ocular movement, facial palsy), tremor, vertigo, memory loss, paresthesia, peripheral neuropathy, peripheral nerve palsy.

**Hypersensitivity Reactions:** An apparent hypersensitivity syndrome has been reported rarely which has included one or more of the following features: anaphylaxis, angioedema, lupus erythematosus-like syndrome, polymyalgia rheumatica, vasculitis, purpura, thrombocytopenia, leukopenia, hemolytic anemia, positive ANA, ESR increase, arthritis, arthralgia, urticaria, asthenia, photosensitivity, fever, chills, flushing, malaise, dyspnea, toxic epidermal necrolysis, erythema multiforme, including Stevens-Johnson syndrome.

**Gastrointestinal:** pancreatitis, hepatitis, including chronic active hepatitis, cholestatic jaundice, fatty change in liver, and, rarely, cirrhosis, fulminant hepatic necrosis, and hepatoma; anorexia, vomiting.

**Reproductive:** gynecomastia, loss of libido, erectile dysfunction.

**Eye:** progression of cataracts (lens opacities), ophthalmoplegia.

**Laboratory Test Abnormalities:** Increases in serum transaminase (ALT, AST) values and CPK have been observed (see WARNINGS).

Transient, asymptomatic eosinophilia has been reported. Eosinophil counts usually returned to normal despite continued therapy. Anemia, thrombocytopenia, and leukopenia have been reported with other HMG-CoA reductase inhibitors.

**Concomitant Therapy:** Pravastatin has been administered concurrently with cholestyramine, colestipol, nicotinic acid, probucol and gemfibrozil. Preliminary data suggest that the addition of either probucol or gemfibrozil to therapy with lovastatin or pravastatin is **not** associated with greater reduction in LDL-cholesterol than that achieved with lovastatin or pravastatin alone. No adverse reactions unique to the combination or in addition to those previously reported for each drug alone have been reported. Myopathy and rhabdomyolysis (with or without acute renal failure) have been reported when another HMG-CoA reductase inhibitor was used in combination with immunosuppressive drugs, gemfibrozil, erythromycin, or lipid-lowering doses of nicotinic acid. Concomitant therapy with HMG-CoA reductase inhibitors and these agents is generally not recommended (see WARNINGS: Skeletal Muscle and PRECAUTIONS: Drug Interactions).

### OVERDOSAGE

There have been no reports of overdoses with pravastatin.

Should an accidental overdose occur, treat symptomatically and institute supportive measures as required.



THE PRAVACHOL® DIRECTION  
IN LIPID MANAGEMENT

Effective lipid management  
doesn't have to be tough



- Improves key lipids — significant reduction in LDL-C<sup>1</sup>
- Excellent safety profile
- Easy for patients — once-daily dosing, well tolerated
- Usual dose: 20 mg once daily at bedtime, with or without food

  
**PRAVACHOL®**  
pravastatin sodium 20 mg tablets

PRAVACHOL is indicated as an adjunct to diet for the reduction of elevated total and LDL-cholesterol levels in patients with primary hypercholesterolemia (Types IIa and IIb) when the response to diet alone has not been adequate. Active liver disease or unexplained transaminase elevations, pregnancy and lactation are contraindications to the use of pravastatin sodium.

Please see CONTRAINDICATIONS, WARNINGS, PRECAUTIONS, and ADVERSE REACTIONS in the brief summary of prescribing information on the adjacent page.



Bristol-Myers Squibb Company



# JOURNAL

OF THE MISSISSIPPI STATE MEDICAL ASSOCIATION

NOVEMBER

1993



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# Discover The Elegance Of A Hybrid



At first glance, it's the *beauty* of a rose that catches the eye. The vibrant color. The delicately shaped petals. But study it more closely, and its *elegance* becomes apparent—a gentle blend of softness and strength.

At first glance, it's the *enhanced performance* of Vaseretic that catches the eye. But study Vaseretic more closely, and its *elegance* becomes apparent. The way its one-tablet, once-a-day dosage minimizes multiple

medications. Minimizes insurance copayments. And minimizes potassium supplementation.

A hybrid *blending of tolerability and power* that's available for the right patient. Vaseretic is indicated for the treatment of hypertension in patients for whom combination therapy is appropriate.

And an elegant discovery for your practice.

**USE IN PREGNANCY:** When used in pregnancy during the second and third trimesters, ACE inhibitors can cause injury and even death to the developing fetus. When pregnancy is detected, Vaseretic® (Enalapril Maleate-Hydrochlorothiazide) should be discontinued as soon as possible. See WARNINGS, Fetal/Neonatal Morbidity and Mortality.

**VASERETIC® 10-25**  
Enalapril Maleate-Hydrochlorothiazide

*Next*

Dosage must be individualized; the fixed combination is not for initial therapy.

Evaluation of the hypertensive patient should always include assessment of renal function.

For a Brief Summary of Prescribing Information, see adjacent pages.



**TABLETS**  
**VASERETIC®**  
(ENALAPRIL MALEATE-HYDROCHLOROTHIAZIDE)

**USE IN PREGNANCY:** When used in pregnancy during the second and third trimesters, ACE inhibitors can cause injury and even death to the developing fetus. When pregnancy is detected, VASERETIC (Enalapril Maleate-Hydrochlorothiazide) should be discontinued as soon as possible. See **WARNINGS, Fetal/Neonatal Morbidity and Mortality.**

**CONTRAINDICATIONS:** VASERETIC is contraindicated in patients who are hypersensitive to any component of this product and in patients with a history of angioedema related to previous treatment with an angiotensin converting enzyme inhibitor. Because of the hydrochlorothiazide component, this product is contraindicated in patients with anuria or hypersensitivity to other sulfonamide-derived drugs.

**WARNINGS:** General: *Enalapril Maleate:* Hypotension: Excessive hypotension was rarely seen in uncomplicated hypertensive patients but is a possible consequence of enalapril use in severely salt/volume depleted persons such as those treated vigorously with diuretics or patients on dialysis.

Syncope has been reported in 1.3 percent of patients receiving VASERETIC. In patients receiving enalapril alone, the incidence of syncope is 0.5 percent. The overall incidence of syncope may be reduced by proper titration of the individual components. (See **PRECAUTIONS, Drug Interactions,** and **ADVERSE REACTIONS.**)

In patients with severe congestive heart failure, with or without associated renal insufficiency, excessive hypotension has been observed and may be associated with oliguria and/or progressive azotemia, and rarely with acute renal failure and/or death. Because of the potential fall in blood pressure in these patients, therapy should be started under very close medical supervision. Such patients should be followed closely for the first two weeks of treatment and whenever the dose of enalapril and/or diuretic is increased. Similar considerations may apply to patients with ischemic heart or cerebrovascular disease, in whom an excessive fall in blood pressure could result in a myocardial infarction or cerebrovascular accident.

If hypotension occurs, the patient should be placed in the supine position and, if necessary, receive an intravenous infusion of normal saline. A transient hypotensive response is not a contraindication to further doses, which usually can be given without difficulty once the blood pressure has increased after volume expansion.

**Angioedema:** Angioedema of the face, extremities, lips, tongue, glottis and/or larynx has been reported in patients treated with angiotensin converting enzyme inhibitors, including enalapril. In such cases VASERETIC should be promptly discontinued and appropriate therapy and monitoring should be provided until complete and sustained resolution of signs and symptoms has occurred. In instances where swelling has been confined to the face and lips the condition has generally resolved without treatment, although antihistamines have been useful in relieving symptoms. Angioedema associated with laryngeal edema may be fatal. Where there is involvement of the tongue, glottis or larynx, likely to cause airway obstruction, appropriate therapy, e.g., subcutaneous epinephrine solution 1:1000 (0.3 mL to 0.5 mL) and/or measures necessary to ensure a patent airway, should be promptly provided. (See **ADVERSE REACTIONS.**)

Patients with a history of angioedema unrelated to ACE inhibitor therapy may be at increased risk of angioedema while receiving an ACE inhibitor (see also **CONTRAINDICATIONS**).

**Neutropenia/Agranulocytosis:** Another angiotensin converting enzyme inhibitor, captopril, has been shown to cause agranulocytosis and bone marrow depression, rarely in uncomplicated patients but more frequently in patients with renal impairment especially if they also have a collagen vascular disease. Available data from clinical trials of enalapril are insufficient to show that enalapril does not cause agranulocytosis at similar rates. Marketing experience has revealed several cases of neutropenia or agranulocytosis in which a causal relationship to enalapril cannot be excluded. Periodic monitoring of white blood cell counts in patients with collagen vascular disease and renal disease should be considered.

**Hydrochlorothiazide:** Thiazides should be used with caution in severe renal disease. In patients with renal disease, thiazides may precipitate azotemia. Cumulative effects of the drug may develop in patients with impaired renal function.

Thiazides should be used with caution in patients with impaired hepatic function or progressive liver disease, since minor alterations of fluid and electrolyte balance may precipitate hepatic coma.

Sensitivity reactions may occur in patients with or without a history of allergy or bronchial asthma.

The possibility of exacerbation or activation of systemic lupus erythematosus has been reported.

Lithium generally should not be given with thiazides (see **PRECAUTIONS, Drug Interactions, Enalapril Maleate and Hydrochlorothiazide**).

**Pregnancy:** *Enalapril-Hydrochlorothiazide:* There was no teratogenicity in rats given up to 90 mg/kg/day of enalapril (150 times the maximum human dose) in combination with 10 mg/kg/day of hydrochlorothiazide (2 1/2 times the maximum human dose) or in mice given up to 30 mg/kg/day of enalapril (50 times the maximum human dose) in combination with 10 mg/kg/day of hydrochlorothiazide (2 1/2 times the maximum human dose). At these doses, fetotoxicity expressed as a decrease in average fetal weight occurred in both species. No fetotoxicity occurred at lower doses; 30/10 mg/kg/day of enalapril-hydrochlorothiazide in rats and 10/10 mg/kg/day of enalapril-hydrochlorothiazide in mice.

When used in pregnancy during the second and third trimesters, ACE inhibitors can cause injury and even death to the developing fetus. When pregnancy is detected, VASERETIC should be discontinued as soon as possible. (See *Enalapril Maleate, Fetal/Neonatal Morbidity and Mortality*, below.)

*Enalapril Maleate, Fetal/Neonatal Morbidity and Mortality:* ACE inhibitors can cause fetal and neonatal morbidity and death when administered to pregnant women. Several dozen cases have been reported in the world literature. When pregnancy is detected, ACE inhibitors should be discontinued as soon as possible.

The use of ACE inhibitors during the second and third trimesters of pregnancy has been associated with fetal and neonatal injury, including hypotension, neonatal skull hypoplasia, anuria, reversible or irreversible renal failure, and death. Oligohydramnios has also been reported, presumably resulting from decreased fetal renal function; oligohydramnios in this setting has been associated with fetal limb contractures, craniofacial deformation, and hypoplastic lung development. Prematurity, intrauterine growth retardation, and patent ductus arteriosus have also been reported, although it is not clear whether these occurrences were due to the ACE-inhibitor exposure or not.

These adverse effects do not appear to have resulted from intrauterine ACE-inhibitor exposure that has been limited to the first trimester. Mothers whose embryos and fetuses are exposed to ACE inhibitors only during the first trimester should be so informed. Nonetheless, when patients become pregnant, physicians should make every effort to discontinue the use of VASERETIC as soon as possible.

Rarely (probably less often than once in every thousand pregnancies), no

10  
mg



25  
mg

alternative to ACE inhibitors will be found. In these rare cases, the mothers should be apprised of the potential hazards to their fetuses, and serial ultrasound examinations should be performed to assess the intraamniotic environment.

If oligohydramnios is observed, VASERETIC should be discontinued unless it is considered lifesaving for the mother. Contraction stress testing (CST), a non-stress test (NST), or biophysical profiling (BPP) may be appropriate, depending upon the week of pregnancy. Patients and physicians should be aware, however, that oligohydramnios may not appear until after the fetus has sustained irreversible injury.

Infants with histories of *in utero* exposure to ACE inhibitors should be closely observed for hypotension, oliguria, and hyperkalemia. If oliguria occurs, attention should be directed toward support of blood pressure and renal perfusion. Exchange transfusion or dialysis may be required as means of reversing hypotension and/or substituting for disordered renal function. Enalapril, which crosses the placenta, has been removed from neonatal circulation by peritoneal dialysis with some clinical benefit, and theoretically may be removed by exchange transfusion, although there is no experience with the latter procedure.

No teratogenic effects of enalapril were seen in studies of pregnant rats, and rabbits. On a mg/kg basis, the doses used were up to 333 times (in rats), and 50 times (in rabbits) the maximum recommended human dose.

**Hydrochlorothiazide: Teratogenic Effects:** Reproduction studies in the rabbit, the mouse and the rat at doses up to 100 mg/kg/day (50 times the human dose) showed no evidence of external abnormalities of the fetus due to hydrochlorothiazide. Hydrochlorothiazide given in a two-litter study in rats at doses of 4 - 5.6 mg/kg/day (approximately 1 - 2 times the usual daily human dose) did not impair fertility or produce birth abnormalities in the offspring. Thiazides cross the placental barrier and appear in cord blood.

**Nonteratogenic Effects:** These may include fetal or neonatal jaundice, thrombocytopenia, and possibly other adverse reactions which have occurred in the adult.

**PRECAUTIONS:** General: *Enalapril Maleate; Impaired Renal Function:* As a consequence of inhibiting the renin-angiotensin-aldosterone system, changes in renal function may be anticipated in susceptible individuals. In patients with severe congestive heart failure whose renal function may depend on the activity of the renin-angiotensin-aldosterone system, treatment with angiotensin converting enzyme inhibitors, including enalapril, may be associated with oliguria and/or progressive azotemia and rarely with acute renal failure and/or death.

In clinical studies in hypertensive patients with unilateral or bilateral renal artery stenosis, increases in blood urea nitrogen and serum creatinine were observed in 20 percent of patients. These increases were almost always reversible upon discontinuation of enalapril and/or diuretic therapy. In such patients renal function should be monitored during the first few weeks of therapy.

Some patients with hypertension or heart failure with no apparent pre-existing renal vascular disease have developed increases in blood urea and serum creatinine, usually minor and transient, especially when enalapril has been given concomitantly with a diuretic. This is more likely to occur in patients with pre-existing renal impairment. Dose reduction of enalapril and/or discontinuation of the diuretic may be required.

**Evaluation of the hypertensive patient should always include assessment of renal function.**

**Hemodialysis Patients:** Anaphylactoid reactions have been reported in patients dialyzed with high-flux membranes (e.g., AN 69) and treated concomitantly with an ACE inhibitor. In these patients consideration should be given to using a different type of dialysis membrane or a different class of antihypertensive agent.

**Hyperkalemia:** Elevated serum potassium (greater than 5.7 mEq/L) was observed in approximately one percent of hypertensive patients in clinical trials treated with enalapril alone. In most cases these were isolated values which resolved despite continued therapy, although hyperkalemia was a cause of discontinuation of therapy in 0.28 percent of hypertensive patients. Hyperkalemia was less frequent (approximately 0.1 percent) in patients treated with enalapril plus hydrochlorothiazide. Risk factors for the development of hyperkalemia include renal insufficiency, diabetes mellitus, and the concomitant use of potassium-sparing diuretics, potassium supplements and/or potassium-containing salt substitutes, which should be used cautiously, if at all, with enalapril. (See **Drug Interactions.**)

**Cough:** Cough has been reported with the use of ACE inhibitors. Characteristically, the cough is nonproductive, persistent and resolves after discontinuation of therapy. ACE inhibitor-induced cough should be considered as part of the differential diagnosis of cough.

**Surgery/Anesthesia:** In patients undergoing major surgery or during anesthesia with agents that produce hypotension, enalapril may block angiotensin II formation secondary to compensatory renin release. If hypotension occurs and is considered to be due to this mechanism, it can be corrected by volume expansion.

**Hydrochlorothiazide:** Periodic determination of serum electrolytes to detect possible electrolyte imbalance should be performed at appropriate intervals. All patients receiving thiazide therapy should be observed for clinical signs of fluid or electrolyte imbalance: hypotension, hypochloremic alkalosis, and hypokalemia. Serum and urine electrolyte determinations are particularly important when the patient is vomiting excessively or receiving parenteral fluids. Warning signs or symptoms of fluid and electrolyte imbalance, irrespective of cause, include dryness of mouth, thirst, weakness, lethargy, drowsiness, restlessness, confusion, seizures, muscle pains or cramps, muscular fatigue, hypotension, oliguria, tachycardia, and gastrointestinal disturbances such as nausea and vomiting.

Hyperkalemia may develop, especially with brisk diuresis, when severe cirrhosis is present, or after prolonged therapy. Interference with adequate oral electrolyte intake will also contribute to hyperkalemia. Hyperkalemia may cause cardiac arrhythmia and may also sensitize or exaggerate the response of the heart to the toxic effects of digitalis (e.g., increased ventricular irritability). Because enalapril reduces the production of aldosterone, concomitant therapy with enalapril attenuates the diuretic-induced potassium loss (see **Drug Interactions, Agents Increasing Serum Potassium**).

Although any chloride deficit is generally mild and usually does not require specific treatment except under extraordinary circumstances (as in liver disease or renal disease), chloride replacement may be required in the

treatment of metabolic alkalosis.

Dilutional hyponatremia may occur in edematous patients in hot weather; appropriate therapy is water restriction, rather than administration of salt except in rare instances when the hyponatremia is life-threatening. In actual salt depletion, appropriate replacement is the therapy of choice.

Hyperuricemia may occur or frank gout may be precipitated in certain patients receiving thiazide therapy.

In diabetic patients dosage adjustments of insulin or oral hypoglycemic agents may be required. Hyperglycemia may occur with thiazide diuretics. Thus latent diabetes mellitus may become manifest during thiazide therapy.

The antihypertensive effects of the drug may be enhanced in the postsympathetomy patient.

If progressive renal impairment becomes evident consider withholding or discontinuing diuretic therapy.

Thiazides have been shown to increase the urinary excretion of magnesium; this may result in hypomagnesemia.

Thiazides may decrease urinary calcium excretion. Thiazides may cause intermittent and slight elevation of serum calcium in the absence of known disorders of calcium metabolism. Marked hypercalcemia may be evidence of hidden hyperparathyroidism. Thiazides should be discontinued before carrying out tests for parathyroid function.

Increases in cholesterol and triglyceride levels may be associated with thiazide diuretic therapy.

**Information for Patients: Angioedema:** Angioedema, including laryngeal edema, may occur especially following the first dose of enalapril. Patients should be so advised and told to report immediately any signs or symptoms suggesting angioedema (swelling of the face, extremities, eyes, lips, tongue, difficulty in swallowing or breathing) and to take no more drug until they have consulted with the prescribing physician.

**Hypotension:** Patients should be cautioned to report lightheadedness especially during the first few days of therapy. If actual syncope occurs, the patients should be told to discontinue the drug until they have consulted with the prescribing physician.

All patients should be cautioned that excessive perspiration and dehydration may lead to an excessive fall in blood pressure because of reduction in fluid volume. Other causes of volume depletion such as vomiting or diarrhea may also lead to a fall in blood pressure; patients should be advised to consult with the physician.

**Hyperkalemia:** Patients should be told not to use salt substitutes containing potassium without consulting their physician.

**Neutropenia:** Patients should be told to report promptly any indication of infection (e.g., sore throat, fever) which may be a sign of neutropenia.

**Pregnancy:** Female patients of childbearing age should be told about the consequences of second- and third-trimester exposure to ACE inhibitors, and they should also be told that these consequences do not appear to have resulted from intrauterine ACE-inhibitor exposure that has been limited to the first trimester. These patients should be asked to report pregnancies to their physicians as soon as possible.

**NOTE:** As with many other drugs, certain advice to patients being treated with VASERETIC is warranted. This information is intended to aid in the safe and effective use of this medication. It is not a disclosure of all possible adverse or intended effects.

**Drug Interactions: Enalapril Maleate: Hypotension—Patients on Diuretic Therapy:** Patients on diuretics and especially those in whom diuretic therapy was recently instituted, may occasionally experience an excessive reduction of blood pressure after initiation of therapy with enalapril. The possibility of hypotensive effects with enalapril can be minimized by either discontinuing the diuretic or increasing the salt intake prior to initiation of treatment with enalapril. If it is necessary to continue the diuretic, provide medical supervision for at least two hours and until blood pressure has stabilized for at least an additional hour. (See **WARNINGS**.)

**Agents Causing Renin Release:** The antihypertensive effect of enalapril is augmented by antihypertensive agents that cause renin release (e.g., diuretics).

**Other Cardiovascular Agents:** Enalapril has been used concomitantly with beta adrenergic-blocking agents, methylglucosides, nitrates, calcium-blocking agents, hydralazine and prazosin without evidence of clinically significant adverse interactions.

**Agents Increasing Serum Potassium:** Enalapril attenuates diuretic-induced potassium loss. Potassium-sparing diuretics (e.g., spironolactone, triamterene, or amiloride), potassium supplements, or potassium-containing salt substitutes may lead to significant increases in serum potassium. Therefore, if concomitant use of these agents is indicated because of demonstrated hypokalemia they should be used with caution and with frequent monitoring of serum potassium.

**Lithium:** Lithium toxicity has been reported in patients receiving lithium concomitantly with drugs which cause elimination of sodium, including ACE inhibitors. A few cases of lithium toxicity have been reported in patients receiving concomitant enalapril and lithium and were reversible upon discontinuation of both drugs. It is recommended that serum lithium levels be monitored frequently if enalapril is administered concomitantly with lithium. Hydrochlorothiazide: When administered concurrently the following drugs may interact with thiazide diuretics:

**Alcohol, barbiturates, or narcotics—**potentiation of orthostatic hypotension may occur.

**Antidiabetic drugs (oral agents and insulin)—**dosage adjustment of the antidiabetic drug may be required.

**Other antihypertensive drugs—**additive effect or potentiation.

**Cholestyramine and colestipol resins—**Absorption of hydrochlorothiazide is impaired in the presence of anionic exchange resins. Single doses of either cholestyramine or colestipol resins bind the hydrochlorothiazide and reduce its absorption from the gastrointestinal tract by up to 85 and 43 percent, respectively.

**Corticosteroids, ACTH—**intensified electrolyte depletion, particularly hypokalemia.

**Pressor amines (e.g., norepinephrine)—**possible decreased response to pressor amines but not sufficient to preclude their use.

**Skeletal muscle relaxants, nondepolarizing (e.g., tubocurarine)—**possible increased responsiveness to the muscle relaxant.

**Lithium—**should not generally be given with diuretics. Diuretic agents reduce the renal clearance of lithium and add a high risk of lithium toxicity. Refer to the package insert for lithium preparations before use of such preparations with VASERETIC.

**Non-steroidal Anti-inflammatory Drugs—**In some patients, the administration of a non-steroidal anti-inflammatory agent can reduce the diuretic, natriuretic, and antihypertensive effects of loop, potassium-sparing and thiazide diuretics. Therefore, when VASERETIC and non-steroidal anti-inflammatory agents are used concomitantly, the patient should be observed closely to determine if the desired effect of the diuretic is obtained.

**Carcinogenesis, Mutagenesis, Impairment of Fertility:** Enalapril in combination with hydrochlorothiazide was not mutagenic in the Ames microbial mutagen test with or without metabolic activation. Enalapril-hydrochlorothiazide did not produce DNA single strand breaks in an *in vitro* alkaline elution assay in rat hepatocytes or chromosomal aberrations in an *in vivo* mouse

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# bone marrow assay.

There was no evidence of a tumorigenic effect when enalapril was administered for 106 weeks to rats at doses up to 90 mg/kg/day (150 times the maximum daily human dose). Enalapril has also been administered for 94 weeks to male and female mice at doses up to 90 and 180 mg/kg/day, respectively, (150 and 300 times the maximum daily dose for humans) and showed no evidence of carcinogenicity.

Neither enalapril maleate nor the active diacid was mutagenic in the Ames microbial mutagen test with or without metabolic activation. Enalapril was also negative in the following genotoxicity studies: reverse mutation assay with *E. coli*, sister chromatid exchange with cultured mammalian cells, and the micronucleus test with mice, as well as in an *in vivo* cytogenetic study using mouse bone marrow.

There were no adverse effects on reproductive performance in male and female rats treated with 10 to 90 mg/kg/day of enalapril.

**Hydrochlorothiazide:** Two-year feeding studies in mice and rats conducted under the auspices of the National Toxicology Program (NTP) uncovered no evidence of a carcinogenic potential of hydrochlorothiazide in female mice (at doses of up to approximately 600 mg/kg/day) or in male and female rats (at doses of up to approximately 100 mg/kg/day). The NTP, however, found equivocal evidence for hepatocarcinogenicity in male mice.

Hydrochlorothiazide was not genotoxic *in vitro* in the Ames mutagenicity assay of *Salmonella typhimurium* strains TA 98, TA 100, TA 1535, TA 1537, and TA 1538 and in the Chinese Hamster Ovary (CHO) test for chromosomal aberrations, or *in vivo* in assays using mouse germinal cell chromosomes, Chinese hamster bone marrow chromosomes, and the *Drosophila* sex-linked recessive lethal trait gene. Positive test results were obtained only in the *in vitro* CHO Sister Chromatid Exchange (clastogenicity) and in the Mouse Lymphoma Cell (mutagenicity) assays, using concentrations of hydrochlorothiazide from 43 to 1300 µg/mL, and in the *Aspergillus nidulans* non-disjunction assay at an unspecified concentration.

Hydrochlorothiazide had no adverse effects on the fertility of mice and rats of either sex in studies wherein these species were exposed, via their diet, to doses of up to 100 and 4 mg/kg, respectively, prior to conception and throughout gestation. **Pregnancy:** Pregnancy Categories C (first trimester) and D (second and third trimesters). See WARNINGS, Pregnancy, Enalapril Maleate, Fetal/Neonatal Morbidity and Mortality. **Nursing Mothers:** Enalapril and enalaprilat are detected in human milk in trace amounts. Thiazides do appear in human milk. Because of the potential for serious reactions in nursing infants from either drug, a decision should be made whether to discontinue nursing or to discontinue VASERETIC, taking into account the importance of the drug to the mother.

**Pediatric Use:** Safety and effectiveness in children have not been established. **ADVERSE REACTIONS:** VASERETIC has been evaluated for safety in more than 1500 patients, including over 300 patients treated for one year or more. In clinical trials with VASERETIC no adverse experiences peculiar to this combination drug have been observed. Adverse experiences that have occurred, have been limited to those that have been previously reported with enalapril or hydrochlorothiazide.

The most frequent clinical adverse experiences in controlled trials were: dizziness (8.6 percent), headache (5.5 percent), fatigue (3.9 percent) and cough (3.5 percent). Adverse experiences occurring in greater than two percent of patients treated with VASERETIC in controlled clinical trials were: muscle cramps (2.7 percent), nausea (2.5 percent), asthenia (2.4 percent), orthostatic effects (2.3 percent), impotence (2.2 percent), and diarrhea (2.1 percent).

Clinical adverse experiences occurring in 0.5 to 2.0 percent of patients in controlled trials included: **Body As A Whole:** Syncope, chest pain, abdominal pain; **Cardiovascular:** Orthostatic hypotension, palpitation, tachycardia; **Digestive:** Vomiting, dyspepsia, constipation, flatulence, dry mouth; **Nervous/Psychiatric:** Insomnia, nervousness, paresthesia, somnolence, vertigo; **Skin:** Pruritus, rash; **Other:** Dyspnea, gout, back pain, arthralgia, diaphoresis, decreased libido, tinnitus, urinary tract infection.

**Angioedema:** Angioedema has been reported in patients receiving VASERETIC (0.6 percent). Angioedema associated with laryngeal edema may be fatal. If angioedema of the face, extremities, lips, tongue, glottis and/or larynx occurs, treatment with VASERETIC should be discontinued and appropriate therapy instituted immediately. (See WARNINGS.)

**Hypotension:** In clinical trials, adverse effects relating to hypotension occurred as follows: hypotension (0.9 percent), orthostatic hypotension (1.5 percent), other orthostatic effects (2.3 percent). In addition syncope occurred in 1.3 percent of patients. (See WARNINGS.)

**Cough:** See PRECAUTIONS, Cough.

**Clinical Laboratory Test Findings; Serum Electrolytes:** See PRECAUTIONS. **Creatinine, Blood Urea Nitrogen:** In controlled clinical trials minor increases in blood urea nitrogen and serum creatinine, reversible upon discontinuation of therapy, were observed in about 0.6 percent of patients with essential hypertension treated with VASERETIC. More marked increases have been reported in other enalapril experience. Increases are more likely to occur in patients with renal artery stenosis. (See PRECAUTIONS.)

**Serum Uric Acid, Glucose, Magnesium, and Calcium:** See PRECAUTIONS. **Hemoglobin and Hematocrit:** Small decreases in hemoglobin and hematocrit (mean decreases of approximately 0.3 g percent and 1.0 vol percent, respectively) occur frequently in hypertensive patients treated with VASERETIC but are rarely of clinical importance unless another cause of anemia coexists. In clinical trials, less than 0.1 percent of patients discontinued therapy due to anemia.

**Liver Function Tests:** Rarely, elevations of liver enzymes and/or serum bilirubin have occurred. Other adverse reactions that have been reported with the individual components are listed below and, within each category, are in order of decreasing severity.

**Enalapril Maleate:** Enalapril has been evaluated for safety in more than 10,000 patients. In clinical trials adverse reactions which occurred with enalapril were also seen with VASERETIC. However, since enalapril has been marketed, the following adverse reactions have been reported: **Body As A Whole:** Anaphylactoid reactions (see PRECAUTIONS, Hemodialysis Patients); **Cardiovascular:** Cardiac arrest; myocardial infarction or cerebrovascular accident, possibly secondary to excessive hypotension in high risk patients (see WARNINGS, Hypotension); pulmonary embolism and infarction; pulmonary edema; rhythm disturbances including atrial tachycardia and bradycardia; atrial fibrillation; hypotension; angina pectoris; **Digestive:** Ileus, pancreatitis, hepatic failure, hepatitis (hepatocellular [proven on rechallenge] or cholestatic jaundice), melena, anorexia, glossitis, stomatitis, dry mouth; **Hematologic:** Rare cases of neutropenia, thrombocytopenia and bone marrow depression. Hemolytic anemia, including cases of hemolysis in patients with G-6-PD deficiency, has been reported, a causal relationship to enalapril has not been established. **Nervous System/Psychiatric:** Depression, confusion, ataxia, peripheral neuropathy (e.g., paresthesia, dysesthesia); **Urogenital:** Renal failure, oliguria, renal dysfunction (see PRECAUTIONS), flank pain, gynecomastia; **Respiratory:** Pulmonary infiltrates, bronchospasm, pneumonia, bronchitis, rhinorrhea, sore throat and hoarseness, asthma, upper respiratory infection; **Skin:** Exfoliative dermatitis, toxic epidermal necrolysis, Stevens-Johnson syndrome, herpes zoster, erythema multiforme, urticaria, pemphigus, alopecia, flushing, photosensitivity; **Special Senses:** Blurred vision, taste alteration, anosmia, conjunctivitis, dry eyes, tearing.

**Miscellaneous:** A symptom complex has been reported which may include a positive ANA, an elevated erythrocyte sedimentation rate, arthralgia/arthritis, myalgia/myositis, fever, serositis, vasculitis, leukocytosis, eosinophilia, photosensitivity, rash and other dermatologic manifestations.

**Fetal/Neonatal Morbidity and Mortality:** See WARNINGS, Pregnancy, Enalapril Maleate, Fetal/Neonatal Morbidity and Mortality.

**Hydrochlorothiazide:** **Body as a Whole:** Weakness; **Digestive:** Pancreatitis, jaundice (intrahepatic cholestatic jaundice), sialadenitis, cramping, gastric irritation, anorexia; **Hematologic:** Aplastic anemia, agranulocytosis, leukopenia, hemolytic anemia, thrombocytopenia; **Hypersensitivity:** Purpura, photosensitivity, urticaria, necrotizing angitis (vasculitis and cutaneous vasculitis), fever, respiratory distress including pneumonitis and pulmonary edema, anaphylactic reactions; **Musculoskeletal:** Muscle spasm; **Nervous System/Psychiatric:** Restlessness; **Renal:** Renal failure, renal dysfunction, interstitial nephritis (see WARNINGS); **Skin:** Erythema multiforme including Stevens-Johnson syndrome, exfoliative dermatitis including toxic epidermal necrolysis, alopecia; **Special Senses:** Transient blurred vision, xanthopsia.

\* Based on patient weight of 50 kg.

For more detailed information, consult your DuPont Pharma Representative or see Prescribing Information.

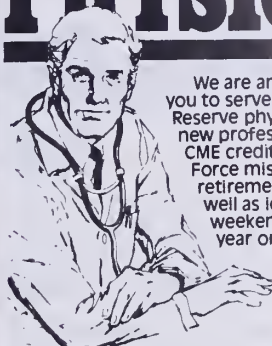
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## SCIENTIFIC ARTICLES

- Laparoscopic Inguinal Herniorrhaphy: Initial Experience In A Community Hospital** 377

*Bruce Pruett, MD*

- Physicochemical Stress In The Production Of Disease** 382

*G. C. Furr, MD*

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## SPECIAL ARTICLE

- The New PRO** 389

*Alton B. Cobb, MD, MPH*

## EDITORIALS

- Doctor, Why Do You Make So Much?** 392

*Don Q. Mitchell, MD*

- MSMA Resolution Calls For Increasing** 393

**Drivers License Age**

*Myron W. Lockey, MD, Editor*

## DEPARTMENTS

- Comment** — James S. McIlwain, Jr., MD 395

- Letter** — Robert D. Currier, MD 397

- Medical Organization** 399

- New Members** 403

- Deaths** 403

- Personals** 405

- Placement Service** 409

- Classified** 410

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## **FLU Shots Encouraged**

Jackson, MS — Most folks label it 'the bug' and often decide to just suffer through it. But for many Americans, influenza can become threateningly expensive and even deadly. In Mississippi, flu and pneumonia combine to rank as the fifth leading cause of death among those over the age of 65. Last year, 707 Mississippians 65 and older died of influenza and pneumonia.

"The flu often escalates from a minor nuisance to a major health problem," said Dr. Mary Currier, state epidemiologist, Mississippi State Department of Health.

Together, the State Department of Health and the Mississippi Chapter of the American Lung Association will combat this year's flu season by encouraging Mississippians to get the influenza vaccination from a county health department, community health center, or private physician. In addition to shielding against two other viral strains, the 1993 flu vaccine guards against the Beijing A strain, already circulating in several neighboring states. Because the State Department of Health gets no state or federal funds for the flu vaccine, county health departments will charge a \$6 fee. Still, no one will be turned away for inability to pay.

Medicare Part B will pay for flu immunization this year as the result of a pilot study conducted two years ago in Mississippi and 19 other states. County health departments can also administer the pneumococcal vaccine for protection against pneumonia.

The Mississippi State Department of Health recommends flu shots for:

- Any person who wants to avoid the flu.
- Certain groups with increased risks for serious complications resulting from the flu, including:
  - Persons 65 years of age or older.
  - Adults and children with chronic disorders of the pulmonary or cardiovascular systems, including children with asthma.
  - Residents of nursing homes and other chronic-care facilities. Adults and children who had medical follow-ups or hospitalization during the previous year because of chronic diseases, blood disorders, kidney problems, or lowered immunity.
  - HIV-infected persons.
  - Children and teenagers from six months to 18 years old who get long-term aspirin therapy and could be at risk of developing Reye syndrome after the flu.
- Health care workers who have contact with high-risk persons in any of the above groups.
- Household members, including children, of persons in a high-risk group.
- Persons preparing to travel to the tropics or the southern hemisphere.
- Persons whose absence from work could result in a disruption of essential services, including school teachers, certain military personnel, police officers, and fire-fighters.

\*\*\*



## **Panel Considers State Worker Pool For Health Coverage**

Jackson, MS — The Governor's Health Care Commission is considering putting teachers, government employees and Medicaid recipients in a single health-insurance pool to provide more coverage to more people.

On the top of the commission's list is a proposal for the Legislature to create a new Health Financing Authority. The agency would create and manage the new health -insurance pool and award regional contracts to doctors and hospitals to provide coverage for those covered by the combined programs.

The goal is to allow uninsured or under-insured Mississippians to receive insurance, Dr. Briggs Hopson of Vicksburg, commission chairman, said.

Mississippians making up to double the federal poverty rate would be eligible to buy into the program.

The Health Finance Authority would have 18 months to develop the program. Ed Ranck, director of the Department of Finance and Administration, estimated the savings of combining the programs would allow an additional 130,000 people to be covered by Medicaid. Dr. Hopson said if all the funds were combined, then "everybody would be guaranteed a minimum benefit package."

\*\*\*

## **State Near Top Policing Practice Of Physicians**

Jackson, MS — Mississippi is the sixth-best state in the nation for policing physicians last year, a report release by the Public Citizen Health Research Group.

The State Board of Medical Licensure took serious disciplinary action against 30 of the Mississippi's 3,846 practicing physicians in 1992, for a rate of 7.80 per 1,000, according to a two-volume list published by the research group. The Washington based group used statistics from the Federation of State Medical Boards.

The nationwide report card contained a list of 10,289 "questionable doctors" — 80 of them in Mississippi — disciplined by states and the federal government since 1986 and 14,574 separate actions.

"I think the state does a wonderful job, especially when you consider this is a profession that has been criticized for lack of policing in the past," said Dr. Walter Rose of Indianola, state licensure board chairman.

Dr. Rose said substance abuse was the most prevalent problem among physicians disciplined by the board in 1992, followed by sub-standard medical treatment and negligence.

The nine-member board monitors the conduct of medical professionals and disciplines them by suspending or revoking their licenses.

"Mississippi has ranked near the top for several years," said Dr. Frank J. Morgan, Jr. of Jackson, executive director of the board, "I don't think this board is more stringent than other boards. But I feel the physicians on the board take their appointments very seriously and mean to protect the public by weeding out bad physicians."

Networking with state and federal regulatory agencies helps the board catch corrupt and troubled physicians, Dr. Morgan said.

\*\*\*

## **HHS Awards Presented for Community Health Promotions**

Washington, DC — Three Mississippi programs will receive national recognition this fall through the Health and Human Services Secretary's 1992 Community Health Promotion Awards.

All nationally honored programs target a special health problem of a community. Problems can include alcohol/drug abuse, smoking, lack of exercise, obesity, teen pregnancy, injury prevention, or any other community health crisis.

Each state submits entries every two years for up to five awards. Awards are given at three levels: Excellence, Letter of Recognition, and Outstanding Service.

Mississippi winners are:

- Gulfport School-Age Child Care Project (Excellence): Through instruction, child care services, and transportation for school-age mothers and their children, 73 percent of these "at-risk" students completed the 1989-90 school year. Eighty percent completed the school year for 1990-91, and no infant deaths occurred.

- DREAM (Outstanding Service): The program used accepted drug prevention strategies, such as involving and training state and community impactors, providing current and factual information, developing life skills, creating alternatives, and influencing policy. DREAM's effects are visible in schools and communities across the state.

- Drug Education and Prevention, Pearl River County (Outstanding Service): Workers referred more than 460 drug users for treatment and logged 11,526 calls for information or crisis intervention. Almost 7,000 residents sought services from the program, and various assemblies reached an audience of 169,017.

Award winners received their plaques, signed by HHS Secretary Donna E. Shalala, at a meeting of the Mississippi Public Health Association on October 7.

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# Laparoscopic Inguinal Herniorrhaphy: Initial Experience In A Community Hospital

Bruce Pruett, MD

**I**nguinal hernia repairs account for over 500,000 surgical procedures annually in the United States.<sup>1</sup> Because the frequency of this procedure is second only to cholecystectomy, surgeons have understandably attempted to transfer the laparoscopic techniques of cholecystectomy to inguinal hernia repair. While laparoscopic cholecystectomy has enjoyed explosive success and popularity, laparoscopic inguinal herniorrhaphy in contrast, has been received with much less enthusiasm and a reluctance on the part of general surgeons to adapt to this new approach to herniorrhaphy. This hesitation is especially unique since laparoscopic herniorrhaphy seems to convey the same benefits and advantages to the patients that made the argument for laparoscopic cholecystectomy so compelling. I will give an historical perspective of this technique and present my initial experience with laparoscopic herniorrhaphy, discuss complications and their management, and attempt to elucidate

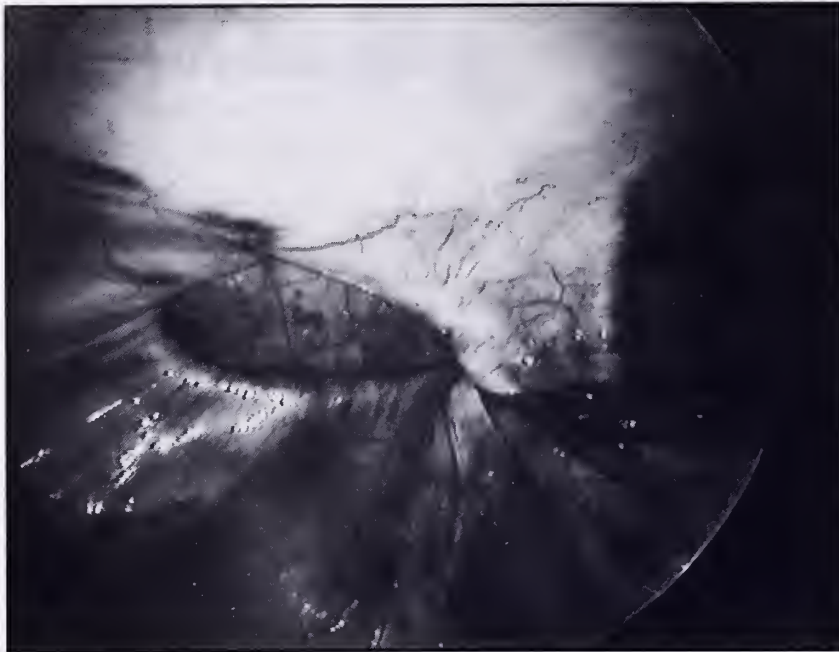
Since February 1992, 32 laparoscopic herniorrhaphies have been performed in 25 patients, including 15 indirect, 16 direct and 1 femoral defect. These were performed in a 275 bed community hospital initially using a "plug and patch" technique, and later employing repair of the hernia defect with a sheet of prolene mesh only. Patients were managed on an out patient basis and were able to resume full activity in 7 to 10 days. Despite the lack of long term follow-up and additional cost basis for the laparoscopic procedures, this method of repairing hernia defects promises to be safe and effective with a high degree of patient satisfaction.

some of the reasons why laparoscopic inguinal repair has been only grudgingly accepted by many experienced general surgeons. My initial series, while limited, gives the perspective of a private practice general surgeon at a 275 bed community hospital.

### Historical Perspective

Most open inguinal hernia repairs are accomplished by the extraperitoneal approach which Bassini first described in 1884.

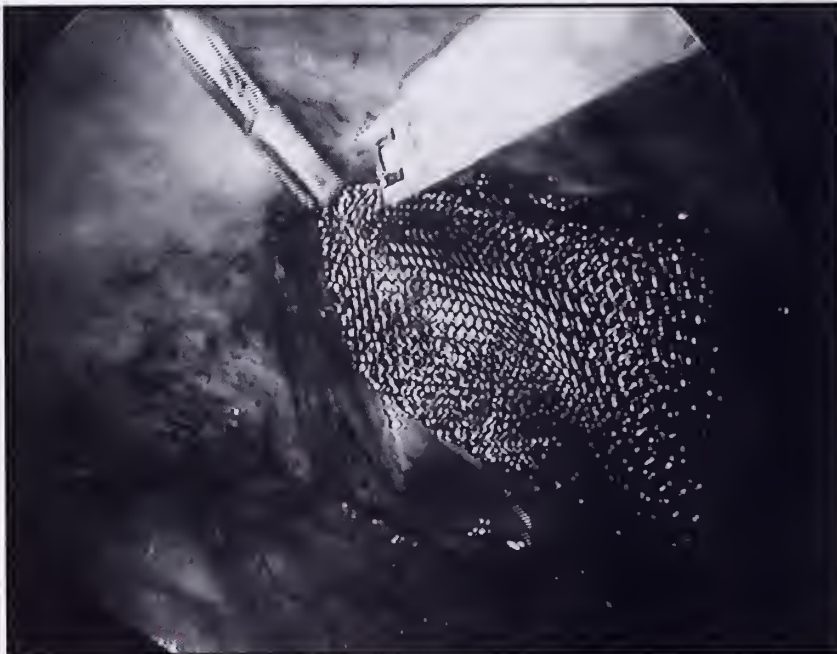
The flaw in this repair is that tissues are approximated under considerable tension, resulting in pain, a significant number of recurrences, and morbidity associated with testicular nerve, and spermatic cord trauma. In 1990, Ger reported a series of thirteen patients with indirect hernias who were repaired laparoscopically using Michel clips to close the internal inguinal ring.<sup>2</sup> Remarkably, there was only one recurrence in this group after a 4 year follow-up. In the same year,



*Figure 1 - Hernia defect as seen through the intraperitoneal camera.*

Popp described a preperitoneal sutureless patch repair in a female patient,<sup>3</sup> and Schultz reported a plug and patch repair using prolene mesh.<sup>4</sup> In 1991, Corbitt related a series of plug repairs with prolene patch preperitoneally,<sup>5</sup> and Fitzgibbons, reported using a patch over the

peritoneum which led to few, and only filmy adhesions, to the exposed prolene patch.<sup>6</sup> Also in 1991, Arregui described a formal preperitoneal dissection with fixation of the mesh by suture.<sup>7</sup> Clearly, rapid advances in the laparoscopic repair of inguinal hernias were occurring. With the



*Figure 2 - Prolene Mesh stapled to Cooper's ligament, pubic tubercle, and transversalis fascia.*

availability of the Endo-Hernia stapler from USSC, enabling surgeons to firmly fix the mesh to the anatomical structures, the number of recurrences were decreasing from the earlier mentioned techniques. Currently, the speed and ease with which the procedure can be done makes it possible for the average general surgeon to become proficient at laparoscopic inguinal hernia repair using a preperitoneal prolene patch firmly fixed to the fascial structures by wire staples and covered with peritoneum.

### **Methods**

General endotracheal anesthesia was used in all cases. Pneumoperitoneum, using insufflated carbon dioxide, was performed with the patients in fairly steep trendelenburg position. A 10 mm trocar and cannula was inserted through an umbilical incision, a 12 mm trocar and cannula were inserted on the side of the hernia lateral to the rectus muscle, and a 5 mm trocar and cannula on the contralateral side. Both indirect and direct hernia defects were managed with the same technique. The peritoneum over the internal inguinal ring and the floor of Hesselbach's triangle was incised with electro-cautery. Blunt dissection with graspers exposed the pubic tubercle medially, Cooper's ligament inferiorly, and the cord structures and inferior epigastric vessels laterally, with the transversalis fascia being seen superiorly. The entire inguinal space was dissected whether the hernia was indirect or direct. After the above mentioned structures were identified, the space was covered with an appropriately cut piece of prolene mesh. This mesh was then stapled to the pubic tubercle medially, the transversalis fascia superiorly, and Cooper's liga-





*Figure 3 - Closure of Peritoneal incision with staples*

ment inferiorly. Laterally, the mesh was not stapled over the cord or iliac vessels in the "Triangle of Doom". All superior and lateral staples should not extend below the level of the iliopubic tract, lateral to the internal inguinal ring as staples placed in this area can result in nerve injury to either the genitofemoral or lateral femoral cutaneous nerve. The use of the articulating, rotating hernia staplers make the firm fixation of the mesh not only possible, but expeditious. The peritoneum was then pulled up over the prolene mesh and stapled closed using the same hernia stapler. At this point, all instruments were removed, the pneumoperitoneum was evacuated and any remnant of air in the scrotum was gently massaged out and vented from the peritoneum prior to removal of the cannulas. Fascial openings of 10 mm and 12 mm cannulae were closed with absorbable sutures and skin incisions were infiltrated with 0.25% Marcaine with Epinephrine and closed with subcuticular sutures. Transparent

adhesive dressings were placed, foley catheters removed and the patient's anesthesia reversed. Toradol 60mg IV was usually given at the end of the case, and this was found to drastically decrease the amount of postop pain and nausea in the recovery room. Patients were discharged the same day with no restriction of activity.

### **Results**

Twenty-five patients have undergone laparoscopic inguinal hernia repair of 15 indirect, 16 direct, and one femoral defect. Four of these were patients with recurrent hernias from previous open conventional hernia repairs. There were 19 men and 6 women, with an age range from 21 to 78 years of age. Of the four patients who had undergone previous Bassini repairs, all reported much less pain and quicker return to full activity with the laparoscopic procedure.

Complications encountered included two recurrences in early patients who had the plug and patch technique prior to the

availability of the hernia staplers. Also one episode of umbilical cellulitis that responded to antibiotics and drainage, and two small lateral injuries to the bladder which were immediately recognized and closed with the USSC 30 mm Endo GIA stapler with the vascular cartridge. As a precaution, both closures were checked by instilling methylene blue and saline into the foley to distend the bladder and check for leakage. Finally, one patient had inadvertent injury to the inferior epigastric vessels while opening the peritoneum with the cautery. Both the inferior epigastric vein and artery were controlled by grasping the vessels and applying Endoclips and cautery. Blood loss was minimal. In none of this series of patients did any neuropathy or cord damage occur. However, care was taken not to place any lateral staples inferior to the iliopubic tract, avoiding the "Neurological No Mans Land".

Overall patient satisfaction was far superior to that usually voiced by patients with open herniorrhaphy.

### **Discussion**

Laparoscopic inguinal hernia repair has evolved from both basic laparoscopic techniques and basic principles of inguinal hernia repair. The most commonly performed laparoscopic repair is the preperitoneal laparoscopic counterpart of the extraperitoneal open Lichtenstein repair. Both procedures use mesh to close the hernia defect with a tension-free repair.

The immediately recognized advantages of laparoscopic repairs are decreased pain and drastically shortened convalescence, with no activity restrictions.

This technique, similar to the

extraperitoneal Lichtenstein repair, should lead to lower recurrence rates over non-Lichtenstein tension-producing repairs.

The disadvantages of the laparoscopic technique are that it requires a skilled laparoscopic surgeon, a general anesthetic, longer OR time, and increased OR supply charges. While this extra expense is theoretically recouped by early return to full work productivity, additional efforts at cost reduction by the instrument manufacturers and the hospitals are still badly needed.

Follow-up in this series of patients is less than two years in all instances. Additional long term follow-up will be necessary to validate the results. However, many other large series of over 200 laparoscopic inguinal hernia repairs are now emerging with low recurrence and complication rates, and promising initial results. With the obvious advantages shared by laparoscopic inguinal herniorrhaphy and laparoscopic cholecystectomy, one might well wonder why surgeons have been reluctant to embrace the hernia procedure. One reason for the hesitancy of most surgeons to begin laparoscopic repair of inguinal hernias is that it requires a totally new operation. In cholecystectomy, the anatomy looks the same and we follow the same procedure whether it is open or laparoscopic. Laparoscopic inguinal herniorrhaphy, however, is accomplished from a different view of the anatomy and with a procedure bearing little resemblance to a conventional "open" repair. This unfamiliar perspective of the anatomical structures combined with the challenge of being a "Nintendo" surgeon can intimidate many a would-be laparoscopic herniorrhapser. While the anatomical challenges are real

and valid, there are a plethora of good courses which are available to the surgeon and will adequately acquaint him with the anatomical structures of concern.

One major concern of most busy private practice general surgeons is time. The main question might be: "Why should I spend extra time in the OR doing a laparoscopic hernia repair when I can do an open Lichtenstein in half the time and possibly a lower incidence of recurrence?" This question will undoubtedly be best answered by the patients, their employers and the third party payers. Some will feel that the patient's time, in terms of productivity regained, is more valuable than the surgeon's extra time in the OR, and that the decrease in the patient's pain and disability will outweigh a surgeon's increased frustration with the learning curve associated with a new procedure. With the looming specter of managed care it may become a mute point for many of the patients. Their federally subsidized health insurance may not cover any procedure other than the one with the lowest price tag. Until then, general surgeons should strive to give their patients the best operation in their hands for the patients' problem and be willing to let go of old traditional procedures as technology provides us with better treatment modalities. □

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# Physicochemical Stress in the Production of Disease

G. C. Furr, MD

*Editor's Note: The following article by Dr. George Furr of Clarksdale, Mississippi is a reprint from the November 1953 issue of the Mississippi Doctor. The paper was originally presented before the Section on Hygiene and Public Health at the eighty-fifth annual session of the Mississippi State Medical Association held in Biloxi, Mississippi, May 10-13, 1953. Dr. Furr, a family physician serving Clarksdale area patients for 49 years, retired in June of this year.*

One way of defining life is as an orderly functioning of enzymes. Disease manifests it self as a disorder, inhibition, or hyperfunction of enzymes. Enzymic reactions and the quantitative determination of enzymes are acquiring more and more importance in clinical medicine. Enzymes are reported to be very complex substances but they can be readily understood when you consider that an enzyme is an organic substance which contains essentially a mineral, a vitamin and a specific protein. It also may contain a mineral, a hormone and a specific protein; or it may be a combination of minerals, vitamins and hormones with a specific protein. A change of any one of these factors changes the character and function of the enzyme. In general, these enzymes control all of the chemical reaction of the body.

Minerals, vitamins and amino acids work together within a single cell to produce enzymes. There are hundreds of enzymes within a single cell and they control directly or indirectly all of its chemical actions. Within the confines of cells many

enzymes are at work all the time, and every one of these cells is constantly producing more than a thousand chemical compounds, if the raw materials are available for such synthesis. The harmony of nature in this cell activity is necessary for health and prevention of disease.

In the living cell, the enzyme is constantly under the influence of all of the factors acting at once and it is difficult to attribute a change in activity to any single influence. There are at least eight separate factors that affect the activity of a given amount of enzyme. These factors are: temperature, substrate concentration, coenzyme concentration, hydrogen ion concentration, inhibitor concentration, oxidation-reduction potential, ionic strength.

Stress, or threatened stress (emotions, exercise, cold, burns, infections, drugs, etc.), acting, either directly from the brain or reflexly through the autonomic nerves, stimulates certain sympathetic nuclei of the hypothalamus--the alarm reaction. The sequence of events seems to be: 1) damaging event, 2) by some means the hypothalamus is stimulated,



3) the impulses travel to the anterior pituitary and result in the release of adrenocorticotrophic hormone, which 4) releases a large amount of adrenal cortical "sugar" hormone; 5) this initiates changes in the body in the direction of preventing the systemic anabolism of tissues. At the same time the "sugar hormone" causes a breakdown of lymphoid tissue with a release of immune globulins which help to combat the damaging event if it is an infection. The interference with anabolism of protoplasm floods the system with all manner of building materials for the anabolism of protoplasm, and these materials are thus made available in large amounts to the site of injury. It is postulated that at the site of injury there is a local stimulating factor which is able to override the general systemic effect of the "sugar" hormone and induce a maximal amount of tissue regeneration. After this "catabolic" phase the patient passes into an "anabolic" phase, during which there is a marked anabolism of tissues in all parts of the system as well as in the local site of injury; this continues until the convalescence is completed. In the "anabolic" phase there is no longer an excess of "sugar" hormone, but instead there is all excess of "nitrogen" hormone.

According to Selye, the individual passes through a succession of steps or phases. First he goes through the shock phase, and then the countershock phase, both of which together are known as the "alarm reaction". After this he goes through a stage in which his resistance to the same type of damaging event is much greater than it was before, but during which his resistance to other types of damaging events is much lowered; and, finally, if the damaging event is continued he enters a stage of exhaustion and ultimately dies, or, if the damaging event is terminated, enters a stage of convalescence and eventually recovers.

Thus the sequence of events in the "adaptation syndrome" can be amplified as follows: The large amount of the "sugar" hormone which is released inhibits the "nitrogen" and the "desoxycorticosterone-like" hormones; this prevents the systemic accumulation of protoplasm and of extracellular fluid. When the excess production of the "sugar" hormone ceases and the inhibitory activity disappears, the "nitrogen" and the "desoxycorticosterone-like" hormones are produced in increased amounts which stimulate the systemic anabolism of protoplasm and the reestablishment of electrolyte and water equilibrium during the period of convalescence. The concept of the "adaptation syndrome" provides another addition to the homeostatic mecha-

nisms which are set in motion in an effort to maintain the most optimal conditions in the individual.

When the concept of the "adaptation syndrome" is applied to clinical medicine, it follows that there is an endocrine component in the manifestations of all disease conditions. Certain acute fulminating infections are usually associated with a profound "alarm reaction." An example of this is infection with meningococci, in which such severe demands are made on the "sugar" hormone production by the adrenal cortex that the gland breaks down with hemorrhage and destruction; this is the Waterhouse-Friedrichsen syndrome.

Many disorders of adaptation occur during the "catabolic" phase of the "adaptation syndrome." In a group of human disease conditions, lesions are present which are similar (if not identical) with the pathologic changes that can be induced in animals by the administration of large doses of desoxycorticosterone, and as a result the suggestion has been advanced that in man these disease states arise because of the excessive production of the "desoxycorticosterone-like" hormone by the adrenal cortex. These disease conditions include particularly disturbances in the cardiovascular system, such as periarteritis nodosa, rheumatic diseases such as rheumatoid arthritis and rheumatic fever, hypertension, and renal arteriolar diseases with nephrosclerosis.

Other human disease conditions in which the evidence suggesting an increase in the production of the "D O C"-like hormone by the adrenal cortex is less clear, but respond to ACTH and cortisone. These include disseminated lupus erythematosus, diffuse collagen diseases, dermatomyositis, scleroderma, psoriasis and psoriatic arthritis, pemphigus, gout, acute nephritis, chronic nephritis, nephrosis, status asthmaticus, bronchial asthma, allergic rhinitis, atopic dermatitis, drug hypersensitivity, and other allergic states, ulcerative colitis, myasthenia gravis, acute alcoholic intoxication, certain hypersensitivity and other allergic states, ulcerative colitis, myasthenia gravis, acute alcoholic intoxication, certain psychiatric states, and certain acute infections.

In some disease conditions, however, the administration of ACTH or of cortisone has either produced no effect or possibly made the patients worse; these include viral hepatitis, tuberculosis, poliomyelitis, certain chronic neurologic disorders, and certain psychiatric states.

Now that the reaction of the body to stress has been reviewed I would like to present a few short reports that are significant to clinical conditions

observed in recent years.

ACTH given to normal adults for one to three weeks the secretion of free hydrochloric acid and pepsin of the stomach juice is greatly increased, 200 percent to 300 percent. The volume of gastric secretion was not increased, but the concentration of these active substances. Gastric ulcer is an important part of the alarm reaction, and repeated administration of ACTH simulates the condition of chronic stress.

Recognition of the specific stimulating effect of ACTH and cortisone upon the stomach may provide some help in understanding of pernicious anemia and the clinical achlorhydrias. Increased adrenal activity probably accompanies or precedes clinical ulcer, and ulcer therapy should include attempts to decrease the activity of the adrenal cortex. Patients with sprue are reported to have adrenal cortex insufficiency.

Disturbances of fluid and electrolyte balance continually confront the clinician in many diseases. The changes which these disorders produce may account for many of the symptoms which the patient exhibits. Metabolic derangements associated with disease processes and frequently observed in diabetes mellitus, chronic nephritis, pyloric obstruction and diarrheal disease are usually well recognized. However, alterations in electrolyte structure based primarily on respiratory dysfunction are less common, and therefore, too often go undetected. Hyperpnea causing respiratory alkalosis might easily be confused with compensatory Kussmaul breathing of metabolic acidosis.

Any alteration in the ability of the lungs to eliminate carbon dioxide properly will produce respiratory acidosis or alkalosis. The underlying abnormality in respiratory acidosis is an increase in blood carbonic acid, which follows elevation of carbon dioxide in the pulmonary alveoli. This may result from: 1) breathing air containing abnormally high percentages of carbon dioxide; and 2) conditions in which elimination of carbon dioxide through the lungs is retarded. This group includes: bronchopneumonia; pulmonary congestion; pulmonary emphysema; morphine narcosis, poliomyelitis; convulsive apnea; pulmonary fibrosis; and laryngeal obstruction. Pulmonary edema caused by toxic irritants or infections may also be included.

Respiratory alkalosis may result from any condition in which hyperventilation occurs as a primary manifestation. Clinically, it is observed in poisoning, meningitis, encephalitis; and hyperpexic states, all of which may exhibit overbreathing due to stimulation of the respiratory center. Other causes

are hysteria, and high altitudes. Regardless of etiology, the basic derangement is reduction of alveolar carbon dioxide tension followed by decrease in blood  $\text{HHCO}_3$ . Therefore, plasma pH is raised, unless  $\text{B. HCO}_3$  is reduced proportionately. The later is accomplished by the following mechanisms: 1) excretion of alkali. Alkali in the form of bicarbonate is excreted in the urine early and in small degree unless other changes such as ketosis cause continued excretion; 2) decreased acid elimination; 3) retention of acid metabolic products (ketone bodies accumulate in the blood and ketonuria may occur); 4) retention of chlorides (Blood chlorides are maintained at normal or raised levels); 5) decreased ammonia formation (This enhances elimination of base).

Recent investigation in Chile upon the effect of cortisone upon experimental mouse tumor metastasis are clear cut and capable of throwing light upon the entire problem of tumor development. The South American workers report that in more than two hundred routine transplantations of a mammary adenocarcinoma in a particular strain of mice, no metastases occurred. Local growth of this tumor was inhibited by cortisone. However, inhibition of the local growth was accompanied by the appearance of multiple metastases.

Various reports recently have described methods of increasing the susceptibility of the common small laboratory animal to a number of bacteria formerly considered non-pathogenic for them. Minneapolis workers have increased the pathogenicity for white mice of several species of microorganisms, by a combination of two therapeutic agents, x-radiation and cortisone. The two administered twenty-four hours before experimental inoculations, considerably enhanced the lethal effects of poliomyelitis virus, a Coxsackie virus, *Candida albicans*, and *Blastomyces dermatitidis*. There seemed to be a synergistic effect. The authors believe that susceptibility to many other organisms can be increased by the same technique, and suggest that they have here a method applicable to study of many diseases, a source of much new bacteriologic information, and a method of study of the phenomena of susceptibility and resistance.

Another technic has been described of shortening the incubating period before onset of paralysis in experimental poliomyelitis, and thus presumably increasing the virulence of the infection. According to Milzer, Weiss and Vanderbloom, pertussis vaccine, diphtheria toxoid, or *Salmonella typhimurium* vaccine, can significantly decrease the incubation period before onset of paralysis in mice



infected with the Lansing strain of poliomyelitis.

Depressed cerebral function is a major complication of excess accumulation of thiocyanate. H. J. M. Barnett, M. V. Jackson and W. B. Spaulding report on eight patients presenting problems in the diagnosis of confusional psychosis. Two died, one of brain stem edema and the other of hyperthermia consistent with a similar lesion. Thiocyanate is a dangerous drug unless patients are closely observed for toxic manifestations and serum levels are estimated frequently.

Thiocyanate effects in hypertension are less dependent on quantitative dosage than on individual blood levels of the drug. Toxic reactions result from accumulation of the drug. Lowering of the basal metabolism rarely to myxedematous degree, improved renal tubular function, and nerve tissue and smooth muscle responses suggest an influence of the anion--SCN on hormonal equilibrium, involving especially the thyroid, pituitary, and adrenal cortex. Decreased thyroid activity, increased amino oxidase enzyme which destroys adrenalin and nor-adrenalin at sympathetic nerve ending.

H<sub>2</sub>S and thiocyanates inhibit the enzyme carbonic anhydrase which is found in RBC and responsible for acceleration of release of CO<sub>2</sub> in lung production of HCL in stomach, and secretion of alkali by pancreas. Also present in gray matter of corde medulla and pons (areas attacked by polio).

Guillain-Barre syndrome, or infections neuronitis is characterized by degeneration of the myelin in the peripheral nerves, spinal ganglia, cord, and brain stem. The main causative factor is not know, but evidence suggests that it is due to a disturbance of the enzyme systems of the neurons.

As the viral particles break down, many liberate toxic components, which must be chemical substances, and which interfere with nutrition or respiration in the host cell.

Hydrogen sulfide occurs in sewer gas, in chemical industries and laboratories. It acts as local irritant. Even high dilutions produce conjunctivitis and roughening of the cornea, and keratitis with blebs and ulcers. More concentrated gas, especially with prolonged exposure, causes irritation and pulmonary edema. In acute poisoning, violent systemic effects predominate, mainly in stimulation of the respiration and spinal convulsive centers; and with higher concentrations, indirect paralysis of the respiratory center. Hydrogen sulfide is much more toxic than is commonly realized. It approaches hydrocyanic acid in toxicity and rapidity of action.

In December, 1952, a four-day fog in London caused about 4,000 deaths. The highest concentra-

tion of smoke was 4.46 mg. per cu. m. and SO<sub>2</sub> 1.399 p.p.m. The *Merck Index*, sixth edition, contains the following: Hydrocarbons, halogenated: carbontetrachloride, chloroform tetrachloroethylene, etc. Warning: Hazardous vapor. These compounds form phosgene in contact with flame or hot metal."

DDT is reported to have a veratrinic action and is thought to affect the sympathomimetic nervous system. Carey and his group have found demyelination of peripheral neurons and acute atrophy of 10 to 30 per cent of the muscle fibers in rats poisoned with DDT. DDT inhibits rat heart cytochrome oxidase in concentrations of 3 to 30 p.p.m. in substrate. Toxephene is suspected to have the medullary excitant effects of camphor—circulatory and respiratory stimulant.

The following is the second in a series of general reports on select aspects of pesticides. It is prompted by the growing general concern over the efficacy and safety of electric vaporizing units for the dispersion of insecticides within buildings. Proponents of this method of insect control claim that it is superior to other available means because of its greater convenience efficiency, and freedom from danger as compared with more conventional methods, such as hand spraying of insecticides. Others have felt that sustained exposure on a workday or longer basis is intrinsically unsound because little is know about the effects of long-term exposure to low concentrations of insecticides in the atmosphere. While brief or occasional exposure appears to be harmless, it is not reasonable to expect that human beings can avoid injury for longer periods year after year to a toxic agent in atmospheric concentrations that kill insects in a few hours. It is further advanced that the resultant injury may be cumulative or delayed, or simulate a chronic disease of another origin, thereby making identification and statistical comparison difficult or impossible.

A high level of cyanide is present in the blood sera of multiple sclerosis. I have noted clinical evidence of cyanide toxicity and an abnormal secretion of thiocyanates ( the detoxification product of cyanides) in a large number of patients since the fall of 1949. An allergy is produced when there is an excess release of histamine. Histamine causes increased permeability of the intestinal wall of the large intestine allowing penetration of toxins into blood stream. There are close connections between substrates and inhibitors of diamine oxidase in carbohydrate metabolism. Recently more detailed information about these relationships was obtained

by showing that histamine inactivates adenosinephosphatase (ATPase). It is possible, therefore, that DO and its inhibitors (thiamin, pyridoxamine) by regulating the concentrates of histamine and other polyamines, may influence the turnover of ATP, which plays a central role in carbohydrate metabolism.

Any defect in the biochemical processes of the brain, especially those concerned with energy transformations, may make itself known by alterations in cerebral function, including personality changes which may be neurotic or psychotic in character. The production of psychotic reactions with ACTH and cortisone invites further study. These hormones disturb enzymatic reactions by altering the electrolyte and water patterns of the body, thus changing the physicochemical environment in which the various enzymes must operate.

Very little attention have been paid to the military disease of arc welders. This condition is a siderosis due to exposure to fumes rich in iron oxide.

Beryllium inhaled as an insoluble oxide in dust form, may also produce a disease characterized by progressive pulmonary granulomatosis. History of exposure is often difficult to establish since the dyspnea, cough and weight loss may be delayed for years after the last contact. And then the signs can be mistaken for silicosis, tuberculosis or sarcoid. Symptoms may be severe with relatively minor roentgenographic findings. Findings may precede symptoms by many years or may not be seen until after the onset of symptoms. Some clays are thought to contain beryllium.

The function of Nissl's granules of bodies described in any textbook of anatomy or physiology is for the purpose of storing up nervous energy which can change with fatigue or rest of the nervous system. These granules are often deficient or absent in the various exhausting diseases or in conditions which have produced bodily fatigue. Nissl's bodies are numerous in the cortical cells when they are at rest they are also found in the sympathetic ganglion cells. These granules disappear during fatigue or after prolonged stimulations of the nerve fibers connected with the cells. With rest they again return to their normal size. That these bodies are responsible for oxygen metabolism in the cell is a known fact.

ACTH reduces the serum iron, possibly shifting it to the reticulo-endothelial system.

Recent evidence indicates that anoxia may play a role in the etiology of retrolental fibroplasia, the blinding disease that has been taking a rising toll

among prematures.

Dyspnea on exertion, tachycardia, edema of the extremities, anginal pain, palpitation and syncope—are symptoms of inadequate supply of oxygen to the different vital areas of the body.

Environmental conditions which subject the body to acute stress cause an increased liberation of ACTH from the pituitary. Excess ACTH causes loss of phosphorous and induces abnormal calcification. The loss of nitrogen in the urine following the administration of cortisone may arise from either accelerated breakdown of body protein or the inhibition of synthesis of tissue proteins from amino acids, which precursors then accumulate and are excreted by the kidney. Administration of cortisone to rabbits inhibits the production of antibodies.

Physiologic trends observed in those exposed to chemicals, being non-specific, may well be produced by any form of physiologic stress. It is important to realize that there is no great difference between the results of continued exposure to chemicals in intensities short of those causing acute organic injury, and the results of prolonged exposure to cold, to lack of oxygen, or to excessive physical labor, or, indeed, to the early stages of infectious or metabolic disease. Even when we pass from the stage of functional changes involved in the "adaption syndrome" to a state of actual organ damage, there is really no fundamental difference between the damage produced by chemicals and that caused by the other types of disease. A chemical, like an infecting organism, may select one organ for its most pronounced action. Often it is more selective than the infecting organism, but the pathologic changes produced do not differ fundamentally from those already noted in infectious disease. However, since, even in obvious poisoning, the functional derangements produced by the chemical are still important, injudicious chemotherapy may be harmful in chemical poisonings to an extent which we are all apt to overlook when, in infectious diseases, we aim to destroy the infecting agent.

By application of the biochemical principles and the reaction to stress, exposure to chemicals may affect body functions either directly or indirectly, thus producing diseases of stress, functional, and metabolic disorder thereby increasing susceptibility and lowering resistance to infection. □

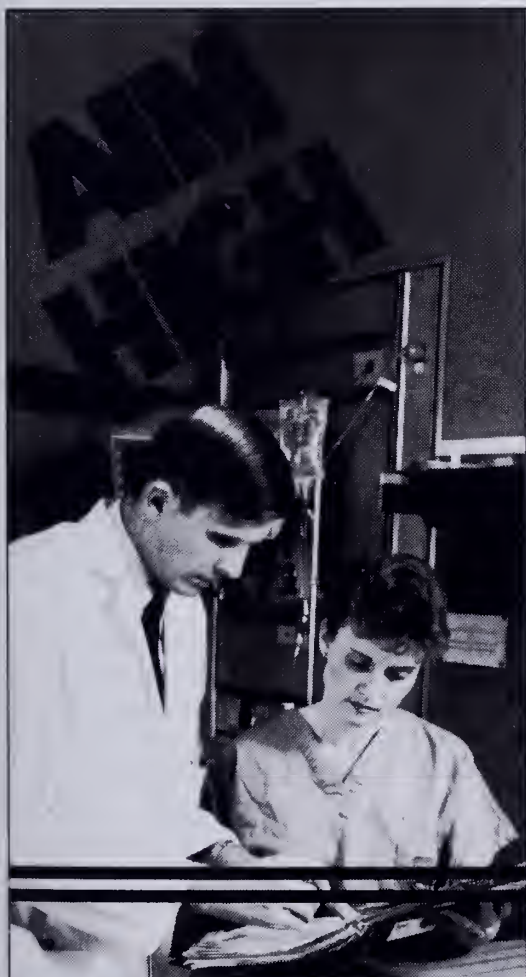
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# The New PRO

**Alton B. Cobb, MD, MPH**  
**Mississippi Foundation for Medical Care**  
**Principal Clinical Coordinator**

**T**he Health Care Financing Administration has embarked on a major project to change the style and the operational methods of each peer review organization (PRO). This new thrust is called the Health Care Quality Improvement Initiative (HCQII).

These changes will have significant impact on the work of hospitals' quality review and assurance functions and the working relationship with the medical staffs. The HCQII is shifting the PRO record review process from a sampling of all records to a pattern analysis of care followed by focused review of patient records.

The changes toward outcome or performance measurement now underway in the program of the JCAHO will dovetail with these new PRO activities; all of this springs from several facts.

Research studies have shown that the traditional PRO approach to quality assurance was faulty in several respects. Among these were the lack of

reliability in conducting record reviews based on a sampling of individual case records. In addition, such random sampling may miss serious quality of care issues which may exist in the hospitals under review. Not insignificant is the widespread existence of negative attitudes by physicians toward these PRO activities.

Other research which has contributed to the new PRO movement is variation analysis and small area analysis. Numerous researchers have conducted studies which show very large variations in the frequencies of different populations having specific medical or surgical procedures performed. For example, the risk or likelihood of people living in one area of a state having surgical interventions for various conditions may vary in several ways. These differences often persist after appropriate adjustments for patient characteristics which may influence the "need" for such procedures. These studies suggest that there

are wide variations in medical practice based on customs, habits, physician and patient discretion, which may not be the optimal patterns for the best patient outcomes.

The clinical guidelines or parameters movement is another mainstay for the new PRO. The use of professionally developed and endorsed clinical guides will generally be more acceptable and appropriate for guiding the changes in care which are indicated than the use of more narrowly drawn criteria and standards for care against which individual case review has been conducted.

Another movement which has influenced both the JCAHO and HCFA is the increasing concern with the best quality at the lowest cost. This has led to an emphasis on outcome or performance measures for evaluating health care versus our sometimes over emphasis on determining the capacity of the system to deliver optimal care. In terms of evaluating hospitals and long-

term care facilities for licensure and certification to provide care under government sponsored programs, we have relied on counting and measuring the overall capacity of the facility rather than looking more at what is happening to patients. Evaluation of quality care in nursing homes has shifted to greater emphasis on outcomes for patients. Increasingly, we are now moving toward the principle that the proof is in the performance as measured by patient outcome indicators and individual patient satisfaction.

Related to these changes is the introduction of the principles for Total Quality Management (TQM) or Continuous Quality Improvement (CQI) into the health care industry.

It is interesting that the beginning of these modern management systems was the work of a Boston surgeon who around 1910 wrote that hospitals should utilize statistical measures to assess quality of care as a set of processes using outcome indicators as measures of success.

The other technological change which is lending its support for these new ways of measuring overall patterns and outcomes for health care is the use of computer data bases and information technology. A number of case adjustment software systems are available and many others are under development which are designed to make comparative analysis of health outcomes between hospitals more reliable and valid. Other systems are developing critical pathways using parameters or clinical guidelines to systematize the decision process.

The basic approaches of this PRO system rest on using information systems and statistical methodology to extract compara-

tive indicators for comparing one hospital or physician's care with others or with the expected outcome after case adjustment. These results rarely if ever will prove that one is better or worse than another, but the identification of such patterns of care will provide the basis for postulating hypotheses to explain why these differences may exist. To verify the actual causes or reasons for the observed differences, focused case or record reviews will be conducted. For example, should a hospital show higher than expected deaths or complications for its acute myocardial infarction cases for that facility, all case records to AMI would be reviewed. The latest clinical guidelines would be utilized in establishing the standards for such focused review. Results from this review would be communicated to the hospital's medical and administrative staff with appropriate recommendations for revised protocols, processes of care, etc.

From these cooperative studies with hospitals and physicians, one would expect to identify some processes of care which through the use of CQI methods may be improved. In addition, some patterns of physician discretion may be subject to educational improvement using current professionally accepted clinical guidelines or parameters and continuing education.

In summary, the New PRO is designed to use modern computer and statistical methodology to identify potential areas for improving the processes and outcomes of health services. Based on patterns of care and outcomes identified, cooperative improvement projects would be undertaken. These would involve the PRO and hospital medical and administrative staffs.

The New PRO is intended to be cooperative, collaborative and educational. It will not be confrontational or punitive.

The principles of CQI teach that we can be more successful in effecting change in systems such as health services through such a collaborative educational approach.

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## **The President's Page**

**DON Q. MITCHELL, MD**

### **Doctor, Why Do You Make So Much?**

**T**hat simple question has caused many mature, intelligent, articulate physicians to quake and quiver and look like "Ned in the first primer". I would include myself in that category - but - not any more. Not since I read a recent editorial by Mike Royko in *The Chicago Tribune*. He gave me the points that I need to be able to address this issue with the general public and stress to my patients.

#### **How much should a person earn if he or she must:**

1. Get excellent grades and a fine education in high school in order to —
2. Be accepted by a good college, spend four years studying hard and maintaining a 3.5 grade point index or better, scoring well on the MCAT, and
3. Spend four more years grinding it out in medical school, often times working and studying 80-100 hours a week, and
4. Spend anywhere from three to eight years in post graduate training depending, upon your specialty, to windup in your mid 30's already deeply in debt (average debt greater than \$50,000 in 1991) and just now entering the job market, and
5. Work under stress, spend many hours on call (nights, week-ends, and holidays) and often have to resolve life threatening medical problems.

*(Continued on page 394)*



## MSMA Resolution Calls For Increasing Drivers License Minimum Age

At the 125th Annual Session of the Mississippi State Medical Association, the Pediatricians of this state introduced, and guided to passage, a resolution addressing the age requirements to obtain a drivers license in Mississippi.

The resolution directs the MSMA and the MSMA Alliance to urge the Governor and the Mississippi Legislature to take the following actions:

1. Raise the minimum age for a drivers license from age 15 to age 16 years,
2. Require the completion of the 9th grade or its equivalent as a pre-requisite for initial licensure and
3. Provide for a driving permit at age 15 when accompanied by a licensed driver 21 years old or older.

This was a bold step by the Pediatricians as this issue is surely a hot potato for politicians. In the comment section, on page 357, of the October 1993, issue of the Journal MSMA, they outlined the data supporting this recommended action.

To be successful it will require involvement of the total MSMA membership from the home turf to the capital.

Success in this endeavor will help reduce the disproportionately high rate of accidents in the 15 year old age group as well as the extreme cost of supporting driving by this age group.

Please commit yourself to actively participating in this action.

**Myron W. Lockey, MD**  
Editor

The editorial opinions expressed in this Journal are those of the indicated author. Editorial opinions are not expressions of the views, or official policies of The Mississippi State Medical Association. We encourage the membership to submit letters for publication regarding any opinion expressed or information contained in the Journal.

Now Doctor, "Do you **really** need to charge that much?" Here are more facts that our patients need to know:

- Only 19% of the total US health spending is for physician services which includes: **overhead expenses now up to 60% or greater in many practices.**

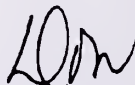
Randall Tobias, chairman and chief executive officer of Eli Lilly & Company, made a comment recently about market pressures with regard to the consumer price of a pharmaceutical product and the actual cost of developing that product. His comment can be easily paraphrased for physicians. As physicians, we face **downward pressures on the price** we can charge for our services and **upward pressures on the cost of delivering** those same services. It is our responsibility to deliver this message loudly and clearly to our patients.

Our patients need to understand that the medical practice and the practice of medicine are not one and the same. The medical practice is a business just like any other business with responsibilities which must be met. I'm aware that when a patient visits a physician's office it is because they are sick and want to see the "doctor"; they don't see the office that is functioning around them in order to facilitate their visit. Somehow we need to bridge the gap between these two impressions.

At this Thanksgiving season we must remember that we, as physicians, have been blessed with God-given talents to care for the sick and injured.

I hope that you and your family take the opportunity to spend time together this Thanksgiving.

Your colleague,



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## Ensuring Quality Under National Health Care Reform

In health care reform the issue is not "can we?" but "we can!" Can we expand access to health care to the nation's 35 million uninsured and control the spiralling cost of the national \$840 billion health care price tag while simultaneously maintaining quality? We can and we must.

Managed competition will only be judged as a success if the quality of care that patients have come to expect from the American health care marketplace is safeguarded. If reform only expands access and controls cost without maintaining quality, few will say that we have done our job of improving our nation's health care system.

As physicians, we have a responsibility to see that quality evaluation and assurance is part of national health care reform. And, as physicians, we also have an imperative to ensure that quality assurance is independent of purchasers with cost-only conflicts; is a professional discipline; and, most importantly, receives the necessary resources to effectively monitor and assess quality treatment.

Some in the Administration and Congress advocate that the state-based Health Alliances be given the task of ensuring quality. But organizations whose primary function is to control costs and negotiate with health plans for the best possible price cannot also be responsible for ensuring the highest quality of care. The inherent and perceived conflicts between controlling costs and ensuring quality are simply inconsistent with the imperatives for public accountability and physician confidence.

Just look at the system we have today. Fragmentation of quality evaluation among purchasers is one of the biggest problems with the current system. This fragmentation creates an administrative burden as physicians try to comply with, and interpret results from, a myriad of proprietary and government entities.

A lack of confidence in quality monitoring and feedback activity also plagues the current system. In part, this emanates from the limitations of a fragmented system, but it also relates to inadequate resource allocation.

As we seek to structure a quality assurance system under a national health care plan, some important criteria must be met.

It must be a system-wide quality assurance program with parallel organizing entities — most likely at the state level — that can provide a coherent, seamless approach to continuous improvement.

Organizations fulfilling this quality assurance function must be well versed and experienced in the newest methods of quality evaluation; be capable of clinically sophisticated data analysis as well as medical review; and, be up to speed on the latest practice guidelines, functional outcome requirements and patient-centered evaluations. Quality assurance cannot just be an add-on responsibility of already overworked providers. It must be a discipline in its own right, with the necessary and appropriate resources.

Quality assurance organizations must be accountable to consumers, but also credible with physicians, nurses, and other health care providers to whom it will provide information and feedback to help improve quality. These organizations will act as consumer watchdogs, but it must also be in partnership with health care professionals to improve outcomes, not to second guess treatment.

Can such an infrastructure capable of supporting quality assurance be part of the national health care reform? As physicians, we have but one response... it can and it must.

**James S. McIlwain, Jr., MD**  
Medical Director  
MS Foundation for Medical Care





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**TO: The Editors and MSMA Membership —****Dear physicians of Mississippi:**

As I retire I wish to thank you for being who you are, for doing what you do, which you do very well, for supporting the neurology department and the medical center over the years, for welcoming us Yankees, and to say that I have enjoyed our relationship. It was 33 years ago this past spring when Marilyn and I first came by to call on Julian and Nancy Youmans. They showed us around a new and pretty medical center, a T-shaped seven story building on a grassy hill, self contained, full of energy and very attractive to a midwesterner who then was in an aging megopolis of a medical center which had trouble relating to the physicians of the state. As we left Jackson in our old Buick up Highway 51, I said to Marilyn that the situation was attractive and if I ever had an offer from this or a similar place I would consider it. That summer Julian wrote that the neurologist in residence had left and the open position was now in the department of Medicine. In the fall I returned and with delight took part in walk rounds with Robert Snavelly, that wonderful chairman of the small superb medical department, which included Allison, Langford, Johnson, McDuffie, Tyler, Blake, Bell, Busie and Campbell and met those in other departments who, working more than full time, provided a good medical education to all with probably one eighth the faculty we have now. So I joined up. Those labor intensive sparkling years generated the strong feeling that we were doing something useful and good in company with the physicians of Jackson and the State, a feeling that persists.

Over the years I would guess that I have interacted with a majority of you one way or another in caring for your patients with neurologic disease at the UMC and VA clinics and hospitals. This has not been a perfect relationship. Many times we have been forced to say that we didn't know what was going on. Or that the clinic was full or there was not a bed for the patient and to fall back on the tired statement that the patient could come to the emergency room and await the freeing up of a bed, an unsatisfactory solution at best. It has been our hope over the years that the filling of the State

with neurologists would ameliorate these situations and it has to a degree. There is no question that the pressure on the UMC beds is less as the State's neurologists and neurosurgeons handle more of the work but I still hear the residents saying the same thing over the phone. We probably still need either more neurologists or beds for those patients who can't afford full private care, a larger problem than I am prepared to consider. When I hear the politicians putting forth various solutions for full medical care I wonder if they will work. The problems are not simple.

The pleasure of living in Jackson and the State of Mississippi, of teaching, research and patient care in this growing Medical Center and of working with you the physicians of the State has been great.

The changeover in the UMC Neurology leadership that has taken place in the last three years, with Dr. James Corbett taking the helm, has the promise of bringing the neurology department up another level of performance. The changes in Neurology typify the recent changes in all departments in the center. We are larger and now have subspecialists in most areas. Growth has been steady with continuous excellent leadership, especially over the last 20 years with Dr. Nelson at the helm. In the long run there is no real reason why your and my medical center here in Mississippi cannot one day become one of the very best in the world. If we keep our eyes on that goal and have as good and steady leadership and support as we have had over the past 40 years it could happen.

My thanks and best wishes to you all.

**Robert D. Currier, MD**  
Jackson, MS

**COMMENTS, LETTERS OR QUERIES....**

The Editors of *Journal MSMA* invite you to comment on any material that appears in or is absent from the publication.

If you have a comment, letter or query please send it to: The Editor, *Journal MSMA*, PO Box 5229, Jackson, MS 39296-5229



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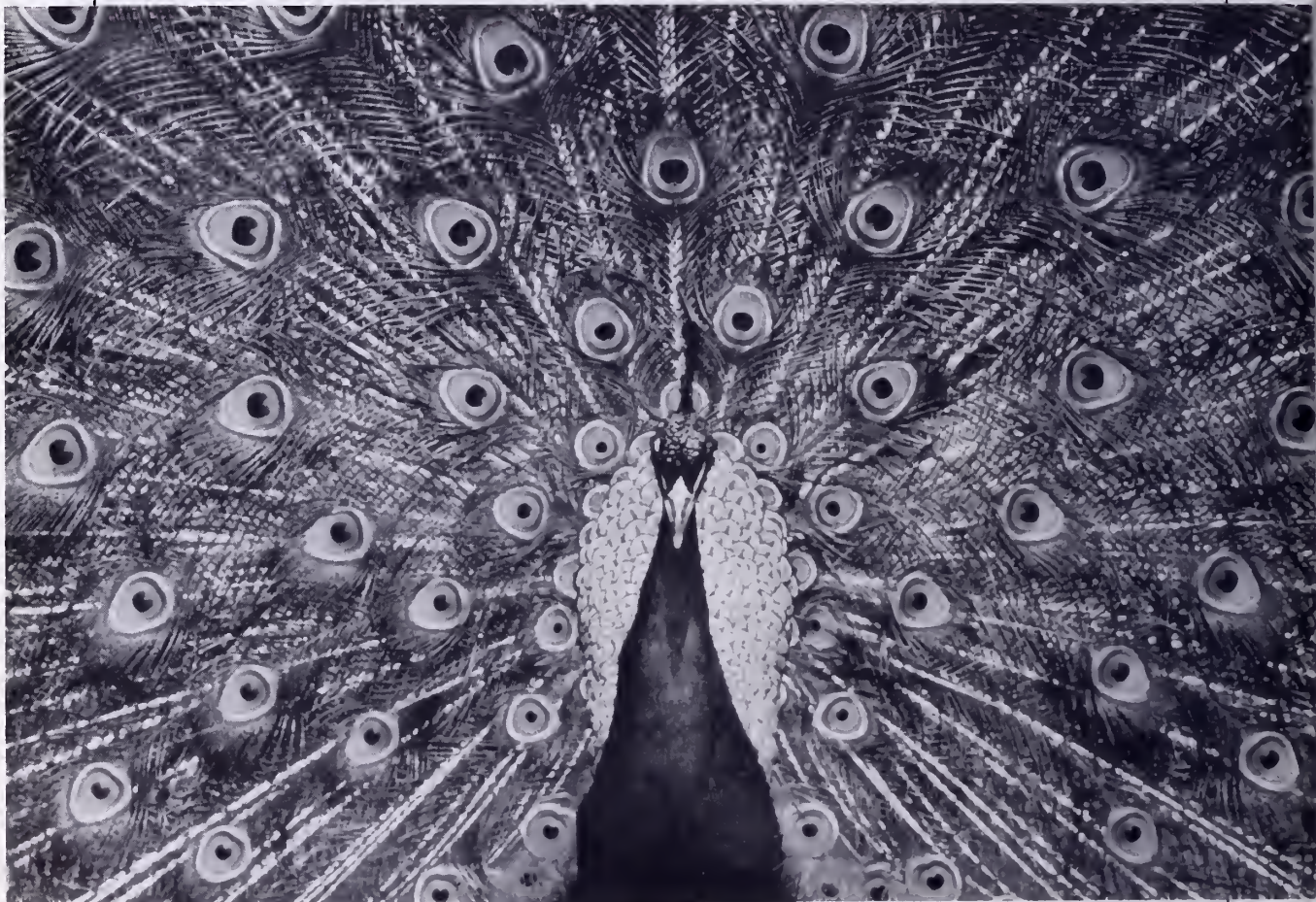
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# Medical Organization

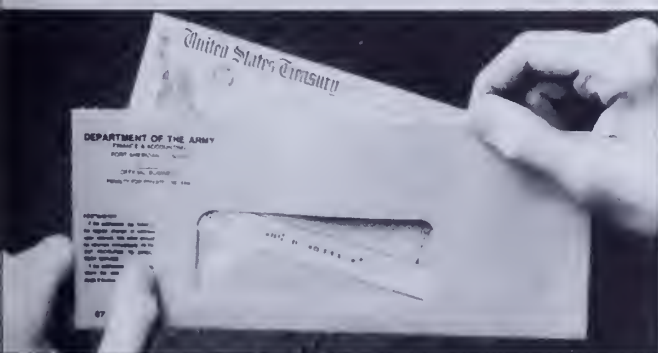
## MSMA Sponsors Managed Care Workshop for Physicians

Saturday, October 9, physicians had the opportunity to participate in a seminar entitled, *Medicine in Transition: Strategies for Change*. Speakers for the workshop included: Barbara Pickelman, owner of the Pickelman Group, a Texas-based consulting firm; Robert K. Alvarez, a partner and health care law specialist with Rick-ey, Bourland, Heflin & Alvarez in Memphis, TN. Dr. Thomas C. Fenter of Jackson served as facilitator for the session and present information on the MS Physicians Care Network.



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## MISSISSIPPI THORACIC SOCIETY HONORS DR. GUY D. CAMPBELL AT ANNUAL MEETING

The Mississippi Thoracic Society honored the late Dr. Guy D. Campbell, Sr., a leading pulmonologist and nationally known lung fungus disease expert at their 1993 Scientific Session/Annual Meeting at the University Medical Center in Jackson by renaming the Boswell lecture the Boswell-Campbell lecture.

The 20th annual Mississippi Lung Association sponsored lecture had been previously named in honor of the late Dr. Henry Boswell, long-time superintendent of the Mississippi State Sanatorium and dean of tuberculosis treatment in Mississippi.

Presenting this year's lecture to 100 Mississippi Thoracic Society members, other physicians and medical students was noted Birmingham, Alabama physician Dick Briggs, Jr. Dr. Briggs' subject was *Obstructive Lung Disease in the 1990's*.

Later in the day, Dr. Briggs presented a paper on *Diagnosis and Management of Interstitial Lung Disease*. Following Dr. Briggs' presentation, various interesting case presentations were presented for review by pulmonologist members of the society.

Also presented at the meeting were the 1993-94 officers for the society. Introduced by out-going president Dr. John Wallace of Laurel were Dr. Jimmy Jones of Jackson, president; Dr. David Westbrook of Jackson, vice president and Dr. Steve Stogner of Hattiesburg, secretary-treasurer. □



The Mississippi Thoracic Society announced its officers for 1993-94 at their Scientific Session/Annual Meeting held recently at the University Medical Center in Jackson. Those elected included Dr. Jimmy Jones of Jackson, President; Dr. David Westbrook of Jackson, vice president; and Dr. Steve Stogner of Hattiesburg, secretary-treasurer. Congratulating Dr. Jones, right, is outgoing MTS President Dr. John Wallace of Laurel.



Special guests at the Annual Meeting of the Mississippi Thoracic Society were family members of the late Dr. Guy Campbell, who was honored by having the former Boswell lecture renamed the Boswell/Campbell lecture, in recognition of his work in pulmonology and lung fungus diseases. Being welcomed by Boswell/Campbell lecturer Dr. Dick Briggs, Jr. (second from right) and MTS President Dr. Jimmy Jones (far right) are Mrs. Guy Campbell, Sr. (second from left) and Dr. Doug Campbell, son of Dr. Guy Campbell Sr.



# The University of Mississippi Medical Center

## Technology Assists Better View Of Inner Space

Technology which explores the stars may soon assist physicians who need a better view of inner space.

Representatives from the John C. Stennis Space Center and other National Aeronautics and Space Administration (NASA) laboratories are collaborating with University of Mississippi Medical Center physicians to see how new technology can give a three dimensional view of a bone fracture and allow surgeons a more detailed view of ulcers lining the stomach.

This is the first joint venture between the state's only space research laboratory and the state's only medical research center.

Other scientists at the Medical Center have worked with other NASA centers — those which study the effects of space travel on biological systems.

But Stennis is primarily a center for the development of propulsion and remote sensing technologies, and Rick Galle, director of technology transfer at Stennis, says the three dimensional view of a bone break and better visualization of the stomach are problems they can solve.

"We develop and use all sorts of imaging techniques to look inside fuel lines and pipes and to analyze the pictures of earth from satellites," Galle said of the Stennis mission to test space shuttle engines.

Dr. Suman Das, professor of surgery and director of the division of plastic surgery at the Medical Center, is the surgeon who wants a way to see a bone break in three dimensions.

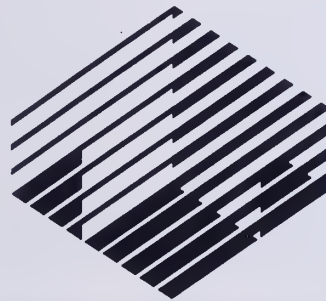
"Being able to see a fracture in three dimensions would be of great benefit to both surgeons and patients," Dr. Das said.

In addition to enhancing the diagnosis and treatment of patients with stomach and diges-

tive problems, a clearer view of the stomach and digestive tract would also lend itself to better teaching, both concerns of Dr. Carol Scott-Conner, professor of surgery at the Medical Center.

Dr. Das initiated the contact with NASA by asking UMC physicians to submit a "problem" list to Galle's office.

"We submitted the list NASA-wide," Galle said. "Everyone who saw the list agreed that these



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researchers were at the cutting edge of their fields, and were knowledgeable about the existing technology. These are the kinds of institutions we like to ally ourselves with," Galle said.

Last year, the center unveiled the results of their collaboration with the Wilmer Eye Institute of Johns Hopkins University in Baltimore, Maryland. Eye specialists at Johns Hopkins contacted the Stennis center with their idea for a vision enhancement system for

the vision impaired.

NASA developed the technology for the system—wrap around video screens—for the computer processing of satellite images. The product should be commercially available within the next year, Galle said.

Other NASA-UMC meetings are planned, said Galle, and the association between the two institutions should make sharing information much easier.

"There's been a growing gap

between technology and medicine," Galle said. "We don't always know how what we've developed can be used in medicine, and researchers aren't always familiar with the technology that's available to help them solve problems."

"Collaborations like ours, which have no other purpose but technology application and development, can bridge that gap," Galle said. □

**THE DELTA REGION AIDS EDUCATION AND TRAINING CENTER** grant is one of 17 federally funded for specialized comprehensive HIV/AIDS Education and Training in Arkansas, Louisiana, and Mississippi. Educational offerings are available in six disciplines - medicine, nursing, dentistry, infection control, mental health, and social work. Physicians, nurses, and health-related professionals are available to visit your area and provide educational services. Please include us in your next meeting. Additional information may be obtained by calling the Division of Infectious Diseases, University of Mississippi Medical Center.

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## New Members

**Collins, Curtis L.**, Jackson. Born Jackson, MS, May 19, 1961; MD, University of Mississippi School of Medicine, Jackson, MS, 1988; interned one year Trover Clinic, Madisonville, KY; pathology residency, University of Arkansas, Little Rock, AR, 1989-93; elected by Central Medical Society.

**Coss, Pacita R.**, Hattiesburg. Born Lucban, Philippines, December 16, 1937; MD, University of Santo Tomas, Manila Philippines, 1962; family practice residency, Tucson Hospitals Medical Education Program, Tucson, AZ, 1967-70 and one year University of Arizona 1991-92; elected by South Mississippi Medical Society.

**House, James R., III**, Jackson. Born Jackson, MS, December 18, 1961; MD, University of Mississippi School of Medicine, Jackson, MS, 1986; internship one year, University Medical Center, Jackson, MS; otolaryngology residency, same, 1987-91; research & clinical fellow, House Ear Institute, Los Angeles, CA, 7/91-12/92; elected by Central Medical Society.

**Lee, Zina D.**, McComb. Born Tribbett, MS, February 18, 1964; MD, University of Mississippi School of Medicine, Jackson, MS, 1990; internal medicine residency, Howard University Hospital, Washington, DC, 1990-93; elected by South Central Medical Society.

**Reed, William Ray, Jr.**, Tupelo. Born Tupelo, MS, April 5, 1961; MD, University of Mississippi School of Medicine, Jackson, MS, 1987; interned one, University Medical Center, Jackson, MS; doctoral research fellowship in radiation biology, University of Iowa, Iowa City, IA, 1988-90; radiation oncology residency, University of Iowa Hospitals and Clinics, Iowa City, IA, 1990-93; elected by Northeast Mississippi Medical Society.

**Shah, Nikhil S.**, Greenville. Born March 23, 1957; MD, Karatiya Medical Colleges, India, 1981; internal medicine residency, Los Angeles County-University of Southern California, Los Angeles, CA, 1987-90; gastroenterology fellowship, University of Missouri Hospital & Clinics, Columbia, MO, 1991-93; elected by Delta Medical Society.

**Turner, Gerald Alan M.**, Columbus. Born Eupora, MS, February

24, 1959; MD, University of Mississippi School of Medicine, Jackson, MS 1989; family practice residency, University Medical Center, Jackson, MS 1989-92; elected by Prairie Medical Society.

### **CORRECTION:**

*September Issue, page 326:*

**Jeffrey Todd Willis**, Collins, MS. One year training in Internal Medicine, UMC, Jackson, MS, 1989-90.

## Deaths

**Buck, William H.**, Jackson. Born October 13, 1923, Bessemer, AL; MD, Tulane University School of Medicine, New Orleans, LA, 1948; interned one year US Public Health Service, San Francisco, CA, 1948-49; died October 12, 1993, age 70.

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## NATIONAL AND REGIONAL

**American Medical Association**, Annual Meeting, June 13 - 17, 1993 Chicago; Interim, December 5 - 8, New Orleans, LA James S. Todd, MD, Executive Vice President, 515 N. State St., Chicago, IL 60610

## STATE AND LOCAL

**Mississippi State Medical Association**, 126th Annual Session, May 11-15, 1994, Jackson, Charles L. Mathews, Executive Director, 735 Riverside Drive, PO Box 5229, Jackson 39296-5229.

**Mississippi Academy of Family Physicians**, Leontine Stevens, Executive Secretary, PO Box 1215 Ridgeland 39158.

**Amite-Wilkinson Counties Medical Society**, 3rd Monday, March, June, September, December, James S. Poole, MD, Secy., The Gloster Clinic, PO Box D, Gloster 39638. Counties: Amite, Wilkinson.

**Central Medical Society**, 1st Tuesday, February, April, October, December, 6:30 p.m., Primos Northgate Restaurant, Jackson. Patsy Douglas, Executive Secy., 735 Riverside Dr., Jackson 39202. Counties: Hinds, Leake, Madison, Rankin, Scott, Simpson.

**Clarksdale and Six Counties Medical Society**, 3rd Wednesday, April, and 1st Wednesday, November, 2:00 p.m., Clarksdale, Glen L. Wegener, MD, Secy., PO Box 430, Clarksdale, MS 38614-0430. Counties: Coahoma, Quitman, Tallahatchie, Tunica.

**Coast Counties Medical Society**, January, March, June, and November. James E. Clarkson, MD, Secy., Mail: Ms. Leslie Johnson, PO Box 128, Biloxi 39533. Counties: Hancock, Harrison.

**Delta Medical Society**, 2nd Wednesday, April and October. Walter H. Rose, MD, Secy., 122 E. Baker St., Indianola 38751. Counties: Bolivar, Humphreys, Leflore, Sunflower, Washington, Yazoo.

**East Mississippi Medical Society**, 1st Tuesday, February, April, June, October, December. Charles L. Wilkinson, MD, Secy., Mail: Ms. Jenkins, PO Box 4053, West Station, Meridian 39305. Counties: Clarke, Kemper, Lauderdale, Neshoba, Newton, Winston.

**Homochitto Valley Medical Society**. Meetings scheduled quarterly. David G. Hall, MD, Secy., 150 Jeff Davis Blvd, Suite 130, Natchez 39120. Counties: Adams, Jefferson.

**North Central District Medical Society**, 3rd Wednesday, March, June, September, January, Gary Holdiness, MD, 332 Hwy 12 W, Kosciusko 39090. Counties: Attala, Carroll, Choctaw, Granada, Holmes, Montgomery, Webster.

**Northeast Mississippi Medical Society**, 1st Thursday, March, June, September, December. Richard L. Heyer, Jr., MD, Secy., Mail: Ms. Shirley Irwin, PO Box 3294, Tupelo 38803-3294. Counties: Alcorn, Calhoun, Chickasaw, Itawamba, Lee, Monroe, Pontotoc, Prentiss, Tishomingo, Union.

**North Mississippi Medical Society**, 1st Thursday, April, September, and 3rd Thursday, January. Catherine E. Gleason, MD, Secy., 1306 Belk Blvd., Oxford 38655. Counties: Benton, Lafayette, Marshall, Panola, Tate, Tippah, Yalobusha.

**Prairie Medical Society**, 2nd Tuesday, March, June, September, December, Joseph S. Boggess, MD, Secy., 515 Willowbrook Rd., Columbus, MS 39701. Counties: Clay, Oktibbeha, Noxubee, Lowndes.

**Singing River Medical Society**, Quarterly, December, March, June and September. Hal Moore, MD, Secy., Mail: Ms. Beverly Small, 3003 Shortcut Rd, Pascagoula 39567. County: Jackson.

**South Central Mississippi Medical Society**, 2nd Tuesday, March, June, September, December. Julian T. Janes, Jr., MD, Secy., PO Box 1910, McComb 39648. Counties: Copiah, Franklin, Lawrence, Lincoln, Pike, Walthall.

**South Mississippi Medical Society**, 2nd Thursday, March, June, September, December. William A. Whitehead, MD, 415 South 28th Ave., Hattiesburg 39401-7246. Counties: Covington, Forrest, George,

Greene, Jasper, Jefferson Davis, Jones, Lamar, Marion, Perry, Smith, Wayne.

**West Mississippi Medical Society**, 2nd Tuesday, January, May, September, November, 6:30 p.m. Maxwell's Restaurant, Vicksburg. Chester Masterson, MD, Secy., 1901 Mission 66, Vicksburg 39180. Counties: Issaquena, Sharkey, Warren.

## Mississippi Institutions and Organizations Accredited for Continuing Medical Education

The following Mississippi institutions and medical organizations have been accredited in accordance with the "Essentials of the Accreditation Council for Continuing Medical Education (ACCME)" and the Council on Medical Education of the MSMA. Information concerning CME programs for physicians offered by these accredited sources may be obtained by writing the Director, Continuing Medical Education, at the individual institution or organization.

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735 Riverside Drive  
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Hattiesburg, MS 39401

Mississippi Baptist Medical Center  
1225 N. State Street  
Jackson, MS 39202

Gulf Coast Community Hospital  
180 DeBuys Rd.  
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Memorial Hospital at Gulfport  
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Gulfport, MS 39501

Baptist Memorial Hospital of North Mississippi  
Highway 7, South  
Oxford, MS 38655

St. Dominic-Jackson Memorial Hospital  
969 Lakeland Dr.  
Jackson, MS 39216

Delta Regional Medical Center  
1400 E. Union  
Greenville, MS 39704

Methodist Hospital  
5001 W. Hardy St.  
Hattiesburg, MS 39401

MS State Department of Health  
PO Box 1700  
Jackson, MS 39215-1700



**Paul M. Allen** of Pascagoula, gave a presentation, Fourth Decade of Oral Contraception, at the Tulane Medical Center Department of Obstetrics and Gynecology on September 23. He was one of 70 visiting faculty members selected nationwide by Health Learning Systems and the University of Minnesota to give such a presentation.

**Robert E. Bailey**, has associated with the Internal Medicine Clinic

of Laurel in the practice of neurology, 1203 Jefferson Street, Laurel.

**Joe D. Edwards** has associated with Dennis W. Rowland at Rankin Children's Group, Crossgates Medical Plaza, 348 Crossgates Boulevard, Suite 2500, Brandon for the practice of Pediatrics.

**Terry M. French** has associate with Meridian Medical Associ-

ates, PA in the practice of Family Medicine, 2024 15th Street, Meridian.

**Frank E. Harman** has associated with Meridian Medical Associates, PA in the practice of Family Medicine, 2024 15th Street, Meridian.

**Robert A. Mallette** has associated with Eye Specialists of Mississippi (formerly Ford-Herrington Eye Clinic) for the

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practice of Cornea and External Disease, Refractive Surgery, Pediatric Ophthalmology and Strabismus, 1190 N. State Street, Suite 403, Jackson.

**Daniel J. McKiever** has associated with Woodie H. Abraham and Benjamin E. Box in the practice of obstetrics and gynecology, 1523- 22nd avenue, Meridian.

**Henry P. Mills, Jr.**, has associated with Mississippi Eyecare Associates, 1421 N. State Street, Suite 302, for the practice of ophthalmology.

**Mitchell J. Myers** announces the opening of his office for the practice of neurology, 2500 Fifth Street North, Columbus.

**Carolyn R. Norman** has associated with Internal Medicine Associates for the practice of internal medicine, 845 South Madison Street, Tupelo.

**Bharat R. Patel** of Laurel, has completed continuing medical education requirements to retain active membership in the American Academy of Family Physicians.

**Harry R. Patel** has associated with George County Hospital and Community Medical Center in the practice of Internal Medicine, Lucedale.

**Alphonse M. Reed** announces the opening of his internal medicine practice, adult and adolescent medicine, 55 Seargent Prentiss Drive, Suite 102 Tracetown.

**Kelly Segars** of Iuka, has completed continuing medical education requirements to retain active membership in the American

## Physicians' Recognition Award



Seven MSMA members were named recipients of the AMA Physicians Recognition Award in September 1993. This award is presented by the American Medical Association to Physicians who have voluntarily completed a specified number of continuing medical education hours. These individuals are presented below by Medical Society.

### CENTRAL MEDICAL SOCIETY

**Thomas Paul Forks, DO**  
**Carol E H Scott-Conner, MD**  
**Eugene G Woods, MD**

### SOUTH MISSISSIPPI MEDICAL SOCIETY

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**William Meredith Temple, MD**

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**Roland Joseph Mestayer, MD**

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can Academy of Family Physicians.

**Thomas E. Vanderloo** has associated with Columbia Family Clinic in the practice of family medicine, 502 Broad Street, Columbia.

**Richard Edwin Waller** of Marks, has completed continu-

ing medical education requirements to retain active membership in the American Academy of Family Physicians.

**W. Paul Wilcox** has associated with Meridian Medical Associates, PA in the practice of Family Medicine, 2024 15th Street, Meridian. □



# Information For Authors

The Journal of The Mississippi State Medical Association welcomes material for publication if submitted in accordance with the following guidelines. Address all correspondence to the Editor, Journal of the Mississippi State Medical Association, P.O. Box 5229, Jackson, MS, 39296-5229. Contact the managing editor with any questions concerning these guidelines.

**Manuscripts** should be of an appropriate length due to the policy of the Journal to feature concise but complete articles. (Some subjects may necessitate exception to this policy and will be reviewed and published at the Editor's discretion.) The language and vocabulary of the manuscript should be understandable and not beyond the comprehension of the general readership of the Journal. The Journal attempts to avoid the use of medical jargon and abbreviations. All abbreviations, especially of laboratory and diagnostic procedures, must be identified in the text. Manuscripts must be typed, double-spaced with adequate margins. (This applies to all manuscript elements including text, references, legends, footnotes, etc.) **The original and one duplicate should be submitted.** The Journal will also accept manuscripts in the form stated above on IBM-compatible floppy diskette. If a diskette accompanies the manuscript, please identify the word processing program used and the file name. Pages should be numbered. An accompanying cover letter should designate one author as correspondent and include his/her address and telephone number. Manuscripts are received with the explicit understanding that they have not been previously published and are not under consideration by any other publication. Manuscripts are subject to editorial revisions as deemed necessary by the editors and to such modifications as to bring them into conformity with Journal style. The authors clearly bear the full responsibility for all statements made and the veracity of the work reported therein.

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of a manuscript is determined by such factors as the quality of the manuscript, perceived interest to Journal readers, and usefulness or importance to physicians. Authors are notified upon the acceptance or rejection of their manuscript. Accepted manuscripts become the property of the Journal and may not be published elsewhere, in part or in whole, without permission from the Journal.

**Title Page** should carry [1] the title of the manuscript, which should be concise but informative; [2] full name of each author, with highest academic degree(s), listed in descending order of magnitude of contribution (only the names of those who have contributed materially to the preparation of the manuscript should be included); [3] a one- to two-sentence biographical description for each author which should include specialty, practice location, academic appointments, primary hospital affiliation, or other credits; [4] name and address of author to whom requests for reprints should be addressed, or a statement that reprints will not be available.

**Abstract**, if included, should be on the second page and consist of no more than 150 words. It is designed to acquaint the potential reader with the essence of the text and should be factual and informative rather than descriptive. The abstract should be intelligible when divorced from the article, devoid of undefined abbreviations. The abstract should contain: [1] a brief statement of the manuscript's purpose; [2] the approach used; [3] the material studied; [4] the results obtained. Emphasize new and important aspects of the study or observations. The abstract may be graphically boxed and printed as part of the published manuscript.

**Key Words** should follow the abstract and be identified as such. Provide three to five key words or short phrases that will assist indexers in cross indexing your article. Use terms from the Medical Subject Heading list from Index Medicus when possible.

**Subheads** are strongly encouraged. They should provide guidance for the reader and serve to break the typographic monotony of the text. The format is flexible but subheads ordinarily include: Methods and Materials, Case Reports, Symptoms, Examination, Treatment and Technique, Results, Discussion, and Summary.

**References** must be double spaced on a separate sheet of paper and limited to a reasonable number. They will be critically examined at the time of review and must be kept to a minimum. All references must be cited in the text and the list should be arranged in order of citation, not alphabetically. Personal Communications and unpublished data should not be included in references, but should be incorporated in the text. The following form should be followed:

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**Example:** Bora LI, Dannem FJ, Stanford W, et al.  
A guideline for blood use during surgery.  
*Am J Clin Pathol* 1979;71:680-692.

#### **Books**

[1] **Author(s).** Use the surname followed by initials without punctuation. The names of all authors should be given unless there are more than three, in which case the names of the first three authors are used followed by "et al." [2] **Title,** Capitalize the first and last word and each word that is not an article, preposition, or conjunction, of less than four letters. [3] **Edition number,** [4] **Editor's name.** [5] **Place of publication,** [6] **Publisher,** [7] **Year,** [8] **Inclusive page numbers.** Do not omit digits.

**Example:** DeGole EL, Spann E, Hurst RA Jr, et al.  
Bedside Examination, in Cardiovascular  
Medicine, ed 2, Smith JT (ed). New York,  
McGraw Hill Co, 1986, pp 23-27.

**Illustrations** should be submitted in duplicate in an envelope (paper clips should not be used on illustrations since the indentation they make may show on reproduction). Legends should be typed, double-spaced on a separate sheet of paper. Photographic material should be high-contrast glossy prints. Patients must be unrecognizable in photographs unless specific written consent has been obtained, in which case a copy of the authorization should accompany the manuscript. All illustrations should be referred to in the body of the text. Omit illustrations which do not increase understanding of text. **Illustrations must be limited to a reasonable number** (four illustrations should be adequate for a manuscript of 4 to 5 typed pages.) The following information should be typed on a label and affixed to the back of each illustration: figure number, title of manuscript, name of senior author, and arrow indicating top.

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**Acknowledgments** are the author's prerogative; however, acknowledgment of technicians and other remunerated personnel for carrying out routine operations or of resident physicians who merely care for patients as part of their hospital duties is discouraged. More acceptable acknowledgements include those of intellectual or professional participation. The recognition of assistance should be stated as simply as possible, without effusiveness or superlatives.

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**Medical Assurance Co. of MS ..... 381  
Medley and Company ..... 394  
Mississippi Methodist Rehabilitation  
Center ..... second cover  
MS Association for Home Care ..... 388  
MS Emergency Association ..... 409  
MS Physicians Insurance Company ..... 4  
MSMA Benefit Plan & Trust ..... 391**

**Premier Printing ..... 402**

**The Doctors' Company ..... 398  
Trustmark ..... 401**

**US Air Force ..... 387  
US Air Force Reserve ..... 3  
US Army Active ..... 399  
US Army Reserve ..... 405**



**Reference:** 1. Jones PH, et al. Once-daily pravastatin in patients with primary hypercholesterolemia: a dose-response study. *Clin Cardiol*. 1991;14:146-151.

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**Pregnancy and lactation.** Atherosclerosis is a chronic process and discontinuation of lipid-lowering drugs during pregnancy should have little impact on the outcome of long-term therapy for primary hypercholesterolemia. Cholesterol and other products of cholesterol biosynthesis are essential components for fetal development (including synthesis of steroids and cell membranes). Since HMG-CoA reductase inhibitors decrease cholesterol synthesis and possibly the synthesis of other biologically active substances derived from cholesterol, they may cause fetal harm when administered to pregnant women. Therefore, HMG-CoA reductase inhibitors are contraindicated during pregnancy and in nursing mothers. **Pravastatin should be administered to women of childbearing age only when such patients are highly unlikely to conceive and have been informed of the potential hazards.** If the patient becomes pregnant while taking this class of drug, therapy should be discontinued and the patient apprised of the potential hazard to the fetus.

## **WARNINGS**

**Liver Enzymes:** HMG-CoA reductase inhibitors, like some other lipid-lowering therapies, have been associated with biochemical abnormalities of liver function. Increases of serum transaminase (ALT, AST) values to more than 3 times the upper limit of normal occurring on 2 or more (not necessarily sequential) occasions have been reported in 1.3% of patients treated with pravastatin in the U.S. over an average period of 18 months. These abnormalities were not associated with cholestasis and did not appear to be related to treatment duration. In those patients in whom these abnormalities were believed to be related to pravastatin and who were discontinued from therapy, the transaminase levels usually fell slowly to pretreatment levels. These biochemical findings are usually asymptomatic although worldwide experience indicates that anorexia, weakness, and/or abdominal pain may also be present in rare patients.

As with other lipid-lowering agents, liver function tests should be performed during therapy with pravastatin. Serum aminotransferases, including ALT (SGPT), should be monitored before treatment begins, every six weeks for the first three months, every eight weeks during the remainder of the first year, and periodically thereafter (e.g., at about six-month intervals). Special attention should be given to patients who develop increased transaminase levels. Liver function tests should be repeated to confirm an elevation and subsequently monitored at more frequent intervals. If increases in AST and ALT equal or exceed three times the upper limit of normal and persist, then therapy should be discontinued. Persistence of significant aminotransferase elevations following discontinuation of therapy may warrant consideration of liver biopsy.

Active liver disease or unexplained transaminase elevations are contraindications to the use of pravastatin (see CONTRAINDICATIONS). Caution should be exercised when pravastatin is administered to patients with a history of liver disease or heavy alcohol ingestion (see CLINICAL PHARMACOLOGY: Pharmacokinetics/Metabolism). Such patients should be closely monitored, started at the lower end of the recommended dosing range, and titrated to the desired therapeutic effect.

**Skeletal Muscle: Rhabdomyolysis with renal dysfunction secondary to myoglobinuria has been reported with pravastatin and other drugs in this class.** Uncomplicated myalgia has also been reported in pravastatin-treated patients (see ADVERSE REACTIONS). Myopathy, defined as muscle aching or muscle weakness in conjunction with increases in creatine phosphokinase (CPK) values to greater than 10 times the upper limit of normal was reported to be possibly due to pravastatin in only one patient in clinical trials (<0.1%). Marked elevation of CPK. Patients should be advised to report promptly unexplained muscle pain, tenderness or weakness, particularly if accompanied by malaise or fever. **Pravastatin therapy should be discontinued if markedly elevated CPK levels occur or myopathy is diagnosed or suspected. Pravastatin therapy should also be temporarily withheld in any patient experiencing an acute or serious condition predisposing to the development of renal failure secondary to rhabdomyolysis, e.g., sepsis; hypotension; major surgery; trauma; severe metabolic, endocrine, or electrolyte disorders; or uncontrolled epilepsy.**

The risk of myopathy during treatment with lovastatin is increased if therapy with either cyclosporine, gemfibrozil, erythromycin, or niacin is administered concurrently. There is no experience with the use of pravastatin together with cyclosporine. Myopathy has not been observed in clinical trials involving small numbers of patients who were treated with pravastatin together with niacin. One trial of limited size involving combined therapy with pravastatin and gemfibrozil showed a trend toward more frequent CPK elevations and patient withdrawals due to musculoskeletal symptoms in the group receiving combined treatment as compared with the groups receiving placebo, gemfibrozil, or pravastatin monotherapy. Myopathy was not reported in this trial (see PRECAUTIONS: Drug Interactions). One patient developed myopathy when clofibrate was added to a previously well tolerated regimen of pravastatin; the myopathy resolved when clofibrate therapy was stopped and pravastatin treatment continued. **The use of fibrates alone may occasionally be associated with myopathy. The combined use of pravastatin and fibrates should generally be avoided.**

## **PRECAUTIONS**

**General:** Pravastatin may elevate creatine phosphokinase and transaminase levels (see ADVERSE REACTIONS). This should be considered in the differential diagnosis of chest pain in a patient on therapy with pravastatin.

**Homozygous Familial Hypercholesterolemia.** Pravastatin has not been evaluated in patients with rare homozygous familial hypercholesterolemia. In this group of patients, it has been reported that HMG-CoA reductase inhibitors are less effective because the patients lack functional LDL receptors.

**Renal Insufficiency:** A single 20 mg oral dose of pravastatin was administered to 24 patients with varying degrees of renal impairment (as determined by creatinine clearance). No effect was observed on the pharmacokinetics of pravastatin or its 3 $\alpha$ -hydroxy isomeric metabolite (SQ 31,906). A small increase was seen in mean AUC values and half-life (t<sub>1/2</sub>) for the inactive enzymatic ring hydroxylation metabolite (SQ 31,945). Given this small sample size, the dosage administered, and the degree of individual variability, patients with renal impairment who are receiving pravastatin should be closely monitored.

**Information for Patients:** Patients should be advised to report promptly unexplained muscle pain, tenderness or weakness, particularly if accompanied by malaise or fever.

**Drug Interactions:** Immunosuppressive Drugs, Gemfibrozil, Niacin (Nicotinic Acid), Erythromycin: See WARNINGS: Skeletal Muscle.

**Antipyrine:** Clearance by the cytochrome P450 system was unaltered by concomitant administration of pravastatin. Since pravastatin does not appear to induce hepatic drug-metabolizing enzymes, it is not expected that any significant interaction of pravastatin with other drugs (e.g., phenytoin, quinidine) metabolized by the cytochrome P450 system will occur.

**Cholestyramine/Colestipol:** Concomitant administration resulted in an approximately 40 to 50% decrease in the mean AUC of pravastatin. However, when pravastatin was administered 1 hour before or 4 hours after cholestyramine or 1 hour before colestipol and a standard meal, there was no clinically significant decrease in bioavailability or therapeutic effect. (see DOSAGE AND ADMINISTRATION: Concomitant Therapy.)

**Warfarin:** In a study involving 10 healthy male subjects given pravastatin and warfarin concomitantly for 6 days, bioavailability parameters at steady state for pravastatin (parent compound) were not altered. Pravastatin did not alter the plasma protein-binding of warfarin. Concomitant dosing did increase the AUC and C<sub>max</sub> of warfarin but did not produce any changes in its anticoagulant activity (i.e., no increase was seen in mean prothrombin time after 6 days of concomitant therapy). However, bleeding and extreme prolongation of prothrombin time has been reported with another drug in this class. Patients receiving warfarin-type anticoagulants should have their prothrombin times closely monitored when pravastatin is initiated or the dosage of pravastatin is changed.

**Cimetidine:** The AUC<sub>0-12h</sub> for pravastatin when given with cimetidine was not significantly different from the AUC for pravastatin when given alone. A significant difference was observed between the AUC's for pravastatin when given with cimetidine compared to when administered with antacid.

**Digoxin:** In a crossover trial involving 18 healthy male subjects given pravastatin and digoxin concurrently for 9 days, the bioavailability parameters of digoxin were not affected. The AUC of pravastatin tended to increase, but the overall bioavailability of pravastatin plus its metabolites SQ 31,906 and SQ 31,945 was not altered.

**Gemfibrozil:** In a crossover study in 20 healthy male volunteers given concomitant single doses of pravastatin and gemfibrozil, there was a significant decrease in urinary excretion and protein binding of pravastatin. In addition, there was a significant increase in AUC, C<sub>max</sub>, and T<sub>max</sub> for the pravastatin metabolite SQ 31,906. Combination therapy with pravastatin and gemfibrozil is generally not recommended.

In interaction studies with aspirin, antacids [1 hour prior to PRAVACHOL (pravastatin sodium)], cimetidine, nicotinic acid, or probucol, no statistically significant differences in bioavailability were seen when PRAVACHOL was administered.

**Other Drugs:** During clinical trials, no noticeable drug interactions were reported when PRAVACHOL was added to diuretics, antihypertensives, digitalis, converting-enzyme inhibitors, calcium channel blockers, beta-blockers, or nitroglycerin.

**Endocrine Function:** HMG-CoA reductase inhibitors interfere with cholesterol synthesis and lower circulating cholesterol levels and, as such, might theoretically blunt adrenal or gonadal steroid hormone production. Results of clinical trials with pravastatin in males and post-menopausal females were inconsistent with regard to possible effects of the drug on basal steroid hormone levels. In a study of 21 males, the mean testosterone response to human chorionic gonadotropin was significantly reduced (p<0.004) after 16 weeks of treatment with 40 mg of pravastatin. However, the percentage of patients showing a  $\geq$ 50% rise in plasma testosterone after human chorionic gonadotropin stimulation did not change significantly after therapy in these patients. The effects of HMG-CoA reductase inhibitors on spermatogenesis and fertility have not been studied in adequate numbers of patients. The effects, if any, of pravastatin on the pituitary-gonadal axis in pre-menopausal females are unknown. Patients treated with pravastatin who display clinical evidence of endocrine dysfunction should be evaluated appropriately. Caution should also be exercised if an HMG-CoA reductase inhibitor or other agent used to lower cholesterol levels is administered to patients also receiving other drugs (e.g., ketoconazole, spironolactone, cimetidine) that may diminish the levels or activity of steroid hormones.

**CNS Toxicity:** CNS vascular lesions, characterized by perivascular hemorrhage and edema and mononuclear cell

infiltration of perivascular spaces, were seen in dogs treated with pravastatin at a dose of 25 mg/kg/day, a dose that produced a plasma drug level about 50 times higher than the mean drug level in humans taking 40 mg/day. Similar CNS vascular lesions have been observed with several other drugs in this class.

A chemically similar drug in this class produced optic nerve degeneration (Wallerian degeneration of retinoganglionic fibers) in clinically normal dogs in a dose-dependent fashion starting at 60 mg/kg/day, a dose that produced mean plasma drug levels about 30 times higher than the mean drug level in humans taking the highest recommended dose (as measured by total enzyme inhibitory activity). This same drug also produced vestibulocochlear (Wallerian-like) degeneration and retinal ganglion cell chromatolysis in dogs treated for 14 weeks at 180 mg/kg/day, a dose which resulted in a mean plasma drug level similar to that seen with the 60 mg/kg dose.

**Carcinogenesis, Mutagenesis, Impairment of Fertility:** In a 2-year study in rats fed pravastatin at doses of 10, 30, or 100 mg/kg body weight, there was an increased incidence of hepatocellular carcinomas in males at the highest dose (p<0.01). Although rats were given up to 125 times the human dose (HD) on a mg/kg body weight basis, their serum drug levels were only 6 to 10 times higher than those measured in humans given 40 mg pravastatin as measured by AUC.

The oral administration of 10, 30, or 100 mg/kg (producing plasma drug levels approximately 0.5 to 5.0 times human drug levels at 40 mg) of pravastatin to mice for 22 months resulted in a statistically significant increase in the incidence of malignant lymphomas in treated females when all treatment groups were pooled and compared to controls (p<0.05). The incidence was not dose-related and male mice were not affected.

A chemically similar drug in this class was administered to mice for 72 weeks at 25, 100, and 400 mg/kg body weight, which resulted in mean serum drug levels approximately 3, 15, and 33 times higher than the mean human serum drug concentration (as total inhibitory activity) after a 40 mg oral dose. Liver carcinomas were significantly increased in high-dose females and mid- and high-dose males, with a maximum incidence of 90 percent in males. The incidence of adenomas of the liver was significantly increased in mid- and high-dose females. Drug treatment also significantly increased the incidence of lung adenomas in mid- and high-dose males and females. Adenomas of the eye Harderian gland (a gland of the eye of rodents) were significantly higher in high-dose mice than in controls.

No evidence of mutagenicity was observed *in vitro*, with or without rat liver metabolic activation, in the following studies: microbial mutagen tests, using mutant strains of *Salmonella typhimurium* or *Escherichia coli*; a forward mutation assay in L5178Y TK +/– mouse lymphoma cells; a chromosomal aberration test in hamster cells; and a gene conversion assay using *Saccharomyces cerevisiae*. In addition, there was no evidence of mutagenicity in either a dominant lethal test in mice or a micronucleus test in mice.

In a study in rats, with daily doses up to 500 mg/kg, pravastatin did not produce any adverse effects on fertility or general reproductive performance. However, in a study with another HMG-CoA reductase inhibitor, there was decreased fertility in male rats treated for 34 weeks at 25 mg/kg body weight, although this effect was not observed in a subsequent fertility study when this same dose was administered for 11 weeks (the entire cycle of spermatogenesis, including epididymal maturation). In rats treated with this same reductase inhibitor at 180 mg/kg/day, seminiferous tubule degeneration (necrosis and loss of spermatogenic epithelium) was observed. Although not seen with pravastatin, two similar drugs in this class caused drug-related testicular atrophy, decreased spermatogenesis, spermatocytic degeneration, and giant cell formation in dogs. The clinical significance of these findings is unclear.

**Pregnancy: Pregnancy Category X:** See CONTRAINDICATIONS.

Safety in pregnant women has not been established. Pravastatin was not teratogenic in rats at doses up to 1000 mg/kg daily or in rabbits at doses of up to 50 mg/kg daily. These doses resulted in 20x (rabbit) or 240x (rat) the human exposure based on surface area (mg/m<sup>2</sup>). However, in studies with another HMG-CoA reductase inhibitor, skeletal malformations were observed in rats and mice. PRAVACHOL (pravastatin sodium) should be administered to women of child-bearing potential only when such patients are highly unlikely to conceive and have been informed of the potential hazards. If the woman becomes pregnant while taking PRAVACHOL, it should be discontinued and the patient advised again as to the potential hazards to the fetus.

**Nursing Mothers:** A small amount of pravastatin is excreted in human breast milk. Because of the potential for serious adverse reactions in nursing infants, women taking PRAVACHOL should not nurse (see CONTRAINDICATIONS).

**Pediatric Use:** Safety and effectiveness in individuals less than 18 years old have not been established. Hence, treatment in patients less than 18 years old is not recommended at this time. (See also PRECAUTIONS: General.)

## **ADVERSE REACTIONS**

Pravastatin is generally well tolerated; adverse reactions have usually been mild and transient. In 4-month long placebo-controlled trials, 1.7% of pravastatin-treated patients and 1.2% of placebo-treated patients were discontinued from treatment because of adverse experiences attributed to study drug therapy, this difference was not statistically significant. In long-term studies, the most common reasons for discontinuation were asymptomatic serum transaminase increases and mild, non-specific gastrointestinal complaints. During clinical trials the overall incidence of adverse events in the elderly was not different from the incidence observed in younger patients.

**Adverse Clinical Events:** All adverse clinical events (regardless of attribution) reported in more than 2% of pravastatin-treated patients in the placebo-controlled trials are identified in the table below, also shown are the percentages of patients in whom these medical events were believed to be related or possibly related to the drug.

Body System/Event	All Events %		Events Attributed to Study Drug %	
	Pravastatin (N = 900)	Placebo (N = 411)	Pravastatin (N = 900)	Placebo (N = 411)
Cardiovascular				
Cardiac Chest Pain	4.0	3.4	0.1	0.0
Dermatologic				
Rash	4.0*	1.1	1.3	0.9
Gastrointestinal				
Nausea/Vomiting	7.3	5.6	2.9	3.4
Diarrhea	6.2	5.6	2.0	1.9
Abdominal Pain	5.4	6.9	2.0	3.9
Constipation	4.0	7.1	0.1	5.1
Flatulence	3.3	3.6	2.7	3.4
Heartburn	2.9	1.9	2.0	0.7
General				
Fatigue	3.8	3.4	0.3	1.0
Chest Pain	3.7	1.9	0.3	0.2
Influenza	2.4*	2.4	0.0	0.0
Musculoskeletal				
Localized Pain	10.0	9.0	1.4	1.5
Myalgia	2.7	1.0	0.6	0.0
Nervous System				
Headache	6.2	3.9	1.7*	0.2
Dizziness	3.3	3.2	1.0	0.5
Renal/Genitourinary				
Urinary Abnormality	2.4	2.9	0.7	1.2
Respiratory				
Common Cold	7.0	6.3	0.0	0.0
Rhinitis	4.0	4.1	0.1	0.0
Cough	2.6	1.7	0.1	0.0

\*Statistically significantly different from placebo.

The following effects have been reported with drugs in this class:

**Skeletal:** myopathy, rhabdomyolysis.

**Neurological:** dysfunction of certain cranial nerves (including alteration of taste, impairment of extra-ocular movement, facial palsy), tremor, vertigo, memory loss, paresthesia, peripheral neuropathy, peripheral nerve palsy.

**Hypersensitivity Reactions:** An apparent hypersensitivity syndrome has been reported rarely which has included one or more of the following features: anaphylaxis, angioedema, lupus erythematosus-like syndrome, polymyalgia rheumatica, vasculitis, purpura, thrombocytopenia, leukopenia, hemolytic anemia, positive ANA, ESR increase, arthritis, arthralgia, urticaria, asthenia, photosensitivity, fever, chills, flushing, malaise, dyspnea, toxic epidermal necrolysis, erythema multiforme, including Stevens-Johnson syndrome.

**Gastrointestinal:** pancreatitis, hepatitis, including chronic active hepatitis, cholestatic jaundice, fatty change in liver, and, rarely, cirrhosis, fulminant hepatic necrosis, and hepatoma; anorexia, vomiting.

**Reproductive:** gynecomastia, loss of libido, erectile dysfunction.

**Eye:** progression of cataracts (lens opacities), ophthalmoplegia.

**Laboratory Test Abnormalities:** increases in serum transaminase (ALT, AST) values and CPK have been observed (see WARNINGS).

Transient, asymptomatic eosinophilia has been reported. Eosinophil counts usually returned to normal despite continued therapy. Anemia, thrombocytopenia, and leukopenia have been reported with other HMG-CoA reductase inhibitors.

**Concomitant Therapy:** Pravastatin has been administered concurrently with cholestyramine, colestipol, nicotinic acid, probucol and gemfibrozil. Preliminary data suggest that the addition of either probucol or gemfibrozil to therapy with lovastatin or pravastatin is **not** associated with greater reduction in LDL-cholesterol than that achieved with lovastatin or pravastatin alone. No adverse reactions unique to the combination or in addition to those previously reported for each drug alone have been reported. Myopathy and rhabdomyolysis (with or without acute renal failure) have been reported when another HMG-CoA reductase inhibitor was used in combination with immunosuppressive drugs, gemfibrozil, erythromycin, or lipid-lowering doses of nicotinic acid. Concomitant therapy with HMG-CoA reductase inhibitors and these agents is generally not recommended (See WARNINGS: Skeletal Muscle and PRECAUTIONS: Drug Interactions.)

## **OVERDOSAGE**

There have been no reports of overdoses with pravastatin.

Should an accidental overdose occur, treat symptomatically and institute supportive measures as required.



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Please see CONTRAINDICATIONS, WARNINGS, PRECAUTIONS, and ADVERSE REACTIONS in the brief summary of prescribing information on the adjacent page.



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## SPECIAL ARTICLE

- Vertical Integration, Clinic Without Walls,  
Physician-Hospital Organizations:  
What It Means And Is It Right For You?** 411  
*William F. Roberts, General Counsel and  
Cecil Harper, CPA*

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- A House That "Love Built"** 420

## EDITORIALS

- Carpe Diem** 422  
*Don Q. Mitchell, MD*  
**Thanks, Dean Nelson** 423  
*George Abraham, MD, Associate Editor*

## DEPARTMENTS

- Comment — Murray Feldberg, MD** 425  
**Medical Organization** 427  
**New Members** 433  
**Personals** 434  
**Placement Service** 441  
**Classified** 442

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**AMA Advisers** - 200 N. LaSalle Street, #535, Chicago, IL 60601, 800-525-0864.

**AMA and AMA Membership Hotline** - 515 North State Street, Chicago, IL 60610; 800-AMA-3211.

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# Vertical Integration, Clinic Without Walls, Physician-Hospital Organizations: What It Means And Is It Right For You?

**William F. Roberts**  
General Counsel  
Mississippi State Medical Association

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**D**uring the last few years the health care system has undergone some very fundamental and profound changes. This will undoubtedly continue, regardless of the nature and degree of overall system reform ultimately enacted by Congress.

The changes that have occurred have been driven by efforts to reduce the cost of health care on the part of insurers, businesses and individuals responsible for paying for all or a portion of such care. Purchasers of health care services are increasingly looking for "value" in the expenditure of their health care dollars. "Value" can be defined as an effort to maximize quality and patient service, while minimizing per patient costs.

**The Emergence of Managed Care As the Principal Means of Achieving "Value"** - in an effort to receive value in expenditures for health care services many businesses and individual purchasers have turned to some form of "managed care".

In the early 1970s, about 90 percent of the U.S. population was covered by indemnity insurance products. By 1991 only 10 to 15 percent of the population had a traditional indemnity insurance policy. After excluding the some 15% of the uninsured, the remaining 75 - 80 percent of the population is covered under some form of

managed care or managed fee-for-service product. Even if Congress does nothing in the area of health system reform, it is estimated that by the turn of the century approximately 90 percent of the population will receive their health care through some managed care entity.

In its purest form, managed care today involves the collaboration of health care providers, principally physicians and hospitals, working together to manage patient care in an effort to maximize quality and reduce per patient costs. Some would argue that most of the efforts heretofore have concerned themselves primarily with the latter, but with increased business and consumer emphasis on receiving "value" those managed care plans that don't stress quality equally with cost aren't likely to survive in the highly competitive environment that lies ahead.

**"Marketshare" As the Mantra for Health Care Delivery** - As managed care becomes the predominate mode of health care delivery, "marketshare" has become the mantra for survival of competing networks and the individual providers of care who make up those networks. A managed care plan has to have a minimum number of persons contracted to receive their health care services through the plan. A physician has to have a certain

minimum patient base in order for his/her practice to not only survive, but accumulate a reasonable profit. A hospital, likewise, has to have a minimum number of inpatient admissions and outpatient and ancillary services.

Under the health system reform plan proposed by President Clinton and other proponents of "managed competition", almost everyone would receive their care through a small number of approved managed care plans. Consequently, health insurance companies, health care providers and other groups are positioning themselves to organize managed care networks. A health care provider must decide which of these networks will attract the marketshare necessary to ensure their and the networks' survival and join them.

**Hospital Efforts to Centralize Marketshare and Delivery System Control** - During the 1970s approximately 70% of all health care dollars were paid to hospitals, with the remaining 30% going to physicians, pharmacies, nursing homes and other health care providers. By the 1990s the percentage of dollars paid out to these two groups had exactly reversed itself. Now, only about 30% of total health care payments go to hospitals, while the remaining 70% is paid to physicians and all other providers.

As hospitals see the erosion of their economic base from such things as shorter lengths of stay, DRGs, outpatient surgery, etc., they are under increased pressure to stabilize the sources of their revenue. To do this, the hospital has to solidify its relationship, either contractually or otherwise, with the physicians who provide the patients and order the tests that are the sources of hospital revenues. There are several ways that an enterprising hospital can accomplish this — all the way from acquiring the practices of referring physicians to entering into various business arrangements with the medical staff. In this paper we will examine some of these arrangements and discuss their advantages and disadvantages for physicians. We will also review some of the alternative organizational structures that are more physician-driven and oriented toward professional autonomy and independence.

## INTEGRATED DELIVERY SYSTEMS

Vertical integration of health care services involves the delivery of a full spectrum of health services — physician, hospital, pharmaceutical, physical and occu-

pational therapy, DME, etc. — by a coordinated entity. Integrated delivery systems may be organized in one of several ways, but typically they provide a full spectrum of "seamless" health care services. Such systems are also characterized by coordinated case management, utilization review and quality assurance, and the exchange of data between system providers.

Vertically integrated delivery systems involve some contractual relationship between the various providers of care within the system. Physicians may own their own practice and simply contract individually or as a group with the hospital to provide care to patients, or the physicians' practices may be purchased by the hospital or some entity that acquires both the hospital and physicians' practices. In the latter case, the hospital and physicians frequently establish a not-for-profit, tax-exempt foundation that purchases both the hospital and the physicians' practices. Under the buy-out arrangement, the physicians typically become employees of either the hospital or the foundation.

## SELLING YOUR PRACTICE

The decision to sell your practice, whether to a hospital or hospital/physician organized foundation, can be an extremely difficult one to make. The hospital or other entity that purchases a physician practice almost always stands to gain, since it assures itself of guaranteed patient referrals. Whether or not the physicians gain anything depends upon several factors.

Physicians who sell their practice are usually motivated by one or a combination of the following: the frustration over coping with the administrative, business and regulatory hassles of running a modern medical practice and desire to devote more time to the clinical aspects of medicine; the desire to maintain a sufficient patient base necessary to ensure a satisfactory income and degree of financial security; and/or the need to infuse some capital into the practice to upgrade its facilities and equipment.

There are several good reasons for selling a medical practice. Among them are:

- \* the arrangement is consistent with your personal and professional goals;
- \* the hospital has a good patient base in a solid service area, it has an aggressive plan for main-



taining viability in a managed care environment, and it has a good contracting network with physicians and other providers;

- \* the hospital, or someone else with whom it contracts, will handle the administrative and business side of the practice; and
- \* it is a good financial arrangement

Similarly, there are also a number of reasons not to sell, such as:

- \* the hospital is in an unstable and highly competitive market;
- \* there may be a loss of professional autonomy associated with becoming an employee of a hospital;
- \* there are alternative, non-hospital affiliated business partners available if the practice is in need of capital infusion;
- \* the sale is motivated principally by a fear that the opportunity to sell may not be available in the future; and
- \* the buy-out price and other financial arrangements are not satisfactory.

### Structuring the Arrangement

As noted earlier, the most common physician practice acquisition by hospitals is where either the hospital, one of its subsidiaries, or its parent company purchases the practice outright. These arrangements customarily involve one of the following: (1) the physician's practice becomes part of the hospital and the physician becomes a hospital employee; (2) the hospital buys the practice and the physician continues to provide service through the practice as an independent contractor; or (3) the hospital purchases the practice assets and takes over administering the practice for a percentage of the revenues.

Another arrangement that has become increasingly popular involves purchase of the practice by a not-for-profit tax exempt foundation that has been established by the hospital for the purpose of owning both the physician practice and often the hospital. The foundation purchases the practice assets, including the medical records. The

foundation takes over the responsibility of running the practice and the physicians either become foundation employees or contract to provide medical care to what becomes the foundation's patients. The principal selling point of the foundation approach is that it enables the practice to access tax-free financing through the sale of tax-exempt bonds to purchase equipment or upgrade the facilities.

### Selling to a Not-For-Profit Hospital or Foundation

Selling your medical practice to a not-for-profit hospital or foundation involves some major requirements necessary for the foundation or hospital to continue to qualify as a tax exempt organization with the Internal Revenue Service (IRS). These primarily involve the critical areas of governance, access to tax-exempt financing through the sale of bonds, and determining the value of the medical practice that is purchased.

In order to gain tax-exempt status from the IRS a foundation or hospital system must operate to benefit community — not private — interests. The IRS views physicians as the private interests that stand to gain the most from efforts to create integrated delivery systems. Accordingly, physicians who have too much control over foundation or hospital governance are viewed by the IRS as likely to further their own, rather than the community's, interests.

To assist its agents in making this assessment the IRS has established a "safe harbor" of physician control: it won't raise the issue of potential physician control as long as physician representation is limited to no more than 20% of the governing board. Although it is rare that a hospital will ever have more than token representation on its governing board, this limitation effectively ensures that the governing board of its foundation will also be dominated by hospital representatives.

The other principal IRS prohibition relates to the purposes for which the money raised through the sale of tax-exempt bonds can be used. According to IRS requirements, 95% of a tax-exempt hospital or foundation's bond proceeds have to be used for activities related to their tax-exempt purposes. That leaves only 5% of the total amount of the bond proceeds available for such things as purchasing equipment for and upgrading facilities of the physicians. This limitation does not, however, apply in situations where the physicians are salaried employees of the hospital or foundation. This reason is frequently used to persuade physicians that they should become hospital employees rather than independent contractors.

## Other Problems to Consider

There are several other factors that should be considered by the physician who is contemplating selling his/her practice to a hospital or foundation:

**Valuing the Practice Assets** - paying a physician more than the market value of the practice may be seen as an inducement for the referral of patients, which is in violation of the "anti-kickback" provisions of the Medicare and Medicaid Fraud and Abuse Act. If greater-than-fair-market value is paid for a practice by a tax-exempt organization it could also be viewed by the IRS as an inurement or benefit for private, rather than public, interests, thereby jeopardizing the tax-exempt status of the hospital or foundation.

Most of the problems related to asset valuation deal with determining the value of the intangible assets of a practice, such as "goodwill". Both the IRS and HHS Inspector General view payments for intangible assets with suspicion and the IRS has a rigorous procedure for determining their value. This limitation on payment for intangible assets is frequently used by the hospital as a reason for reducing the amount it will pay for a practice.

**Compensation** - a physician must be compensated on a reasonable and competitive basis. The hospital or foundation committee that negotiates compensation with physicians must not consist of any physician who is affiliated in any way with the physician whose compensation is being negotiated. The determination of compensation and rates of pay must be an "arms-length transaction".

**Acceptance of Medicare and Medicaid Patients** - physicians who sell their practice to a tax-exempt foundation or hospital will probably have to agree to provide service to all Medicare, Medicaid and charity patients as an indication of the entity's commitment to "benefit the community and public interests" — a necessary element of tax exemption.

**Corporate Practice of Medicine** - many states have specific laws prohibiting anyone other than a "natural" person from practicing medicine. This prohibition serves to bar an entity such as a corporation or hospital from employing physicians to practice medicine as its agent. Mississippi has no statute addressing the issue, and the state Board of Medical Licensure has said it will not concern itself with the employment arrangement of physicians as long as the following are left to the sole and

absolute discretion of the physician:

- the method and manner of treatment
- the means by which patients are treated
- the manner of billing; and
- the amount of fees and expenses to be charged

## PHYSICIAN HOSPITAL ORGANIZATIONS (PHOs)

A PHO is a joint venture between a hospital and members of its medical staff to structure a partially integrated delivery system that can contract with managed care organizations, insurance companies and employers directly. PHOs are principally contracting entities for health care delivery, rather than insurance products which are at risk for underwriting the costs of health care services.

PHOs have been created in response to concerns about reducing health care costs and the competitive forces currently driving the health care marketplace. Some say they are merely an effort by hospitals to lock in market share in their service area and ensure a satisfactory referral stream.

Hospital revenues have declined as more and more patients are treated on an outpatient basis. If one hospital in a multi-hospital service area offers an integrated delivery system to insurers and employers, eventually the other hospitals will follow in order to effectively compete for patients in the local market. Similarly, PHO organization by the only hospital in a service area is usually a competitive response to insurers or others offering managed care products to employers in the area.

### Are PHOs a Competitive Model?

As noted earlier, a PHO is chiefly a delivery system as opposed to an insurance product that bears all or a portion of the risk associated with the cost of providing health care services. Some PHOs are entering into contracts that provide for risk-based capitated payment where physician and hospital costs are bundled together for any number of treatment procedures or diagnoses. Many view this kind of hospital and physician financial integration as inevitable if a vertically integrated delivery system is to be a viable competitor in the managed care market.

Employers have become frustrated with paying thousands of dollars in insurance premiums every month to provide health care coverage for their employees when



they have little or no control over how the money is spent. As a result, they are increasingly looking for health benefit plans that put them in partnership with providers in managing health care expenditures. Many feel that, in order to be truly competitive in a managed care market, PHOs will have to move from merely being contracting entities and delivery systems to assuming some of the financial risk with employers for the costs of care they provide.

### **The Divergent Needs in Hospital-Physician Risk Ventures**

The need to be at risk in order to be competitive in a managed care market could make the PHO model a problem for physicians. In order for the physicians under such an arrangement to minimize their risk and even make a profit the number of inpatient days must be kept to a minimum. The hospital, on the other hand, needs to maximize inpatient days in order to maximize revenues. Consequently, physicians in such a venture must ensure that they manage patient care both appropriately and efficiently while resisting the hospital's need to increase bed occupancy and the provision of ancillary services.

An integrated delivery system, such as a PHO, that is established for the principal purpose of filling hospital beds is doomed to failure from the standpoint of both risk and competitiveness.

### **Who's In Charge?**

Physicians should insist that a PHO governing board have equal representation between the hospital and physicians. That is not enough, however, to ensure that decisions will be made on a democratic basis.

The bylaws of most organizations provide that a majority of directors at a board meeting shall constitute a quorum and a majority vote of those present shall be sufficient for official action. Let's assume that a PHO board consists of six physicians and an equal number of hospital representatives. At a meeting of the board all six hospital representatives are in attendance, but only one physician director is present. The hospital obviously controls the votes on all actions taken at that meeting and those actions may or may not be in the best interests of physicians. For this reason, the PHO bylaws should be written to require that actions of the board of directors, such as approving a managed care contract, must be approved by a majority vote of both the physicians and hospital representatives on the board.

Two things are extremely important in order to

ensure that a PHO truly represents a collaborative, cooperative joint venture between physicians and a hospital. First, the physicians in such a venture must organize themselves to speak collectively in their dealings with the hospital. Nothing will bring down a PHO faster than internecine warfare between the physician members, or the perception that their representatives in governance of the PHO are merely pawns of the hospital.

Secondly, the physicians and hospital should equally contribute to capitalization of the PHO. If the hospital puts up the bulk of the funds it will likely end up calling all the shots on the grounds that it has more to lose. Equalizing the investment at least puts both groups on equal footing at the outset.

### **Friend or Foe?**

Is the establishment of a PHO a good thing? It depends. Properly structured and capitalized, with the right specialty mix and with realistic goals a PHO can offer a lot of advantages to both physicians and hospitals, particularly in managed care contracting. Under the PHO rubric a group of physicians and a hospital can form a single, integrated negotiating unit that can compete with insurers and other managed care organizations in contracting to provide health care to employers and others in the local community.

On the other hand, if the PHO is established mainly for the purpose of filling hospital beds, has unrealistic expectations about its market potential, fails to maintain the necessary physician-hospital balance in decision-making, doesn't make a serious commitment to doing third generation utilization management, and lacks sufficient primary care physicians it could be a huge failure.

## **CLINIC WITHOUT WALLS**

With the rise in vertically integrated delivery systems and decline in profit margins many solo practitioners are concerned about their ability to maintain a viable medical practice in a managed care environment. There are several options available, such as:

- becoming an employed physician with a managed care organization;
- becoming employed by a hospital or other health system;

- joining a single or multi-specialty group practice; or
- forming a new group practice with other physicians.

For the solo, independent practitioner, or even the two or three person practice, affiliation with other physicians to achieve the economies and efficiencies of group practice offers an attractive alternative. There are several ways this can be accomplished.

- a large group practice can acquire one or more solo or small group practices in the same or surrounding communities;
- several solo or small group practices can merge and form a fully integrated single or multi-specialty group practice;
- several independent practices can form a Mutual Services Corporation, sometimes referred to as a Medical Services Organization, in order to combine their billing, employment, accounting, purchasing and other business operations while maintaining independent clinical practices; or
- several independent practices can establish a "Clinic Without Walls" where the physicians effectively integrate their practices and become employees of the new entity, yet maintain their separate, existing practice locations.

### **The Level of Practice Integration**

If several independent practitioners get together to talk about affiliating their practices under some arrangement other than a complete merger into a single group practice they will have to decide to what extent they want, or are willing, to integrate their practices. The level of practice integration is the key factor in determining whether they form a Mutual Services Corporation or a true Clinic Without Walls.

### **The Mutual Services Corporation**

A Mutual Services Corporation (MSC) is an entity that is jointly owned by physicians to manage the day-to-day business and administrative affairs of their respective medical practices. The MSC affords the physicians the advantages of group practice economies of scale by combining various business opera-

tions without integrating other aspects of their practices.

In the typical MSC the physician participants pay a fee, usually monthly, for the various services provided by the entity. The services provided by the MSC to its physicians may include any or all of the following:

- billing and collections
- data collection and analysis
- purchasing
- utilization review and quality assurance
- coverage arrangements
- marketing
- physician recruitment
- practice management

The formation of a Mutual Services Corporation offers physicians several advantages in achieving certain operational efficiencies and reducing duplicative administrative and business costs. By the same token, because there is only a partial integration of the various practices of the participating physicians it may not offer all of the benefits of group practice. Some of these shortcomings are:

- an absence of the level of economic and practice integration between the individual medical practices necessary to avoid anti-trust problems can severely impair the ability of the MSC to negotiate with third party payors and managed care entities on behalf of its physicians;
- some physicians are reluctant to turn over any of their business and administrative operations to the MSC, so they end up increasing, rather than reducing their overhead by essentially paying duplicate costs for these services;
- unlike a fully integrated group practice, it is extremely difficult for the MSC to own and operate various ancillary health services and facilities because of federal "self-referral" prohibitions.

### **Clinic Without Walls**

Many physicians think that a Mutual Services Corporation and Clinic Without Walls are one-and-



the-same, or that they have formed a Clinic Without Walls when what they really have is a Mutual Services Corporation.

As mentioned previously, an MSC simply provides administrative services for its participating physicians. On the other end of scale, however, a true Clinic Without Walls becomes what is, for all intents and purposes, a group practice. The physicians are employed by the new group entity, although they continue to practice in their existing geographic locations. Because the Clinic Without Walls consists of individual physicians who have economically integrated and merged their practices into one corporate entity, the structure not only provides all of the services commonly offered by an MSC, but it can also determine the amount of fees to be charged by its physicians and handle all negotiations with payers and other providers, such as hospitals.

A Clinic Without Walls is frequently formed by a group of independent physicians who wish to integrate and merge their respective practices, but lack the capital to construct a single modern practice facility and equip it with the latest medical technology. Very often the physicians in a Mutual Services Corporation will decide to take the final step in integrating their practices and become a Clinic Without Walls.

### Organizing a Clinic Without Walls

Setting up a Clinic Without Walls will usually involve the following:

- a new corporate entity is chartered and a professional administrator is hired to manage the group affairs;
- a centralized administrative structure is established to handle such functions as billing, collections, payroll, accounting, purchasing, personnel employment, third party negotiations and other practice matters;
- the assets of each of the medical practices, both tangible and intangible, are independently valued in order to determine the amount of stock to be issued to each physician in exchange for signing over the practice assets or making a capital contribution equivalent to the value of the practice;
- the new entity may "purchase" all of the tan-

gible assets, including accounts receivable, of the participating practices through the issuance of stock, or ownership of all or some of the assets may be retained by the individual physicians; and

- employment contracts for each of the physicians are negotiated and prepared, along with agreements for other employment benefits such as insurance, bonuses, retirement, etc. This necessarily involves development of an acceptable compensation plan.

### Anti-Trust Considerations

Any group of physicians considering formation of either a Mutual Services Corporation or Clinic Without Walls should have competent legal counsel with anti-trust experience involved from the outset.

Section 1 of the federal Sherman Act is violated when competitors act in concert and agree or conspire to restrain trade or competition. In the context of health care, agreements between competing physicians to (1) fix prices or the terms of prices, or (2) refuse to contract with or "boycott" a third party are considered *per se* violations of the Sherman Act. However, to the extent that there is substantial professional and economic integration among competitors, such as physicians, the participants will be viewed as joint venturers and any agreements, if properly structured, between the joint venturers that might otherwise be anti-competitive will be viewed as pro-competitive.

The level of professional and economic integration necessary to avoid anti-trust scrutiny should be substantial, although it need not be total integration as exists in group practices. Based on advisory opinions of the Justice Department and Federal Trade Commission and other legal articles, a combination of the following activities would probably suggest the presence of an acceptable level of integration between the participants in a Clinic Without Walls :

1. Creation of a new medical services delivery product through:
  - a. development of new programs for the coordination of care, such as geographic dispersion of participating providers, multi-specialty coverage and shared medical information;

- b. development of quality assurance and utilization management programs;
  - c. development and use of outcomes and cost data;
  - d. the use of joint data processing and medical information systems; and
2. Economic integration through
- a. capital contributions by participating physicians;
  - b. risk sharing through capitation or with-hold agreements;
  - c. joint billing, collections, purchasing and marketing; and
  - d. joint investment in the administrative support systems, such as office equipment and personnel.

If competing providers want to affiliate, but are unwilling to commit to the kind of professional and economic integration necessary to qualify as a legitimate joint venture for anti-trust purposes, there are serious risks involved if they agree on anything relative to prices or fees, or even share such information. This is the Achilles heel of Mutual Service Corporations. A group of otherwise independent physicians cannot simply plop a corporate structure, whether an MSC or a Clinic Without Walls, over their practices and expect to negotiate with payors and managed care organizations free of anti-trust scrutiny. Serious attention must be paid to the level of practice integration present in the venture, both professionally and economically.

Every physician contemplating participation in the development of either a Mutual Services Corporation or Clinic Without Walls should first ask, "is this venture pro-competitive as opposed to anti-competitive"? For instance, if all the specialists in a particular market, such as Jackson, want to form an MSC solely to achieve certain administrative efficiencies and economies of scale in order to reduce operating costs, such a venture would likely not be viewed as anti-competitive.

On the other hand, if the same specialists in a

given market organize an MSC or Clinic Without Walls through which they would not only combine various business and administrative functions, but also attempt to negotiate with payors and managed care organizations it will almost surely be viewed as an effort to fix prices, achieve market power or boycott purchasers.

### **Consider Your Objectives and Options**

As we have seen, there is no set formula for integrating health care delivery systems and no single approach is right for every physician. For some physicians, selling their practice to and becoming an employee of the hospital may be the best means of achieving financial security and professional satisfaction. For others, that may be the least attractive alternative.

Before making a decision about organizing or participating in the formation of any integrated delivery system or restructuring a medical practice, a physician should first determine the objectives of the venture and how they coincide with his or her own professional needs and goals. If the two are incompatible, remember that there are other alternatives. As managed care continues to flourish, new and dynamic practice arrangements will also emerge and physicians will have many options available to them in attempting to maintain a viable, competitive medical practice.

The Mississippi State Medical Association and the American Medical Association have the resources to assist you in assessing your practice and evaluating your options. Physicians can and should serve as the focal point for economic and clinical decision-making in a managed care environment and both MSMA and the AMA can assist you in obtaining the knowledge and informational tools necessary to accomplish that. □



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## A House That "Love Built"

Dr. Bev Evans, Chairman of the Department and Professor of Pediatrics at UMC said, "it is truly a house that love built." As I listened, Dr. Evans began to tell the story of how the Ronald McDonald House located on the University of Mississippi Medical Center Campus became a reality.

Technically, the House was built by Lovebilt, Incorporated, but it was also built and supported by many people, from all walks of life, who have contributed time, money and most of all love to ensure its success.

What is the Ronald McDonald House? More than anything else, Mississippi's Ronald McDonald House is a home. A home where the families of critically ill children can temporarily reside in affordable, comfortable surroundings. It's a place where they can voice their fears and receive the support of others who are in similar circumstances. It is an oasis where they can rest and prepare themselves for the next visit to the pediatric or neo-natal intensive care unit.

Mississippi's Ronald McDonald House began with a sick child and his concerned mother. A little Mississippi boy, who had a serious heart condition, had to be sent



*A wall hanging of Ronald McDonald occupies a prominent position in the house.*

to another state for treatment and his mother stayed nearby at a Ronald McDonald House.

When the child improved and was able to come back to Mississippi to continue his care, his mom went into a local McDonald's restaurant and simply asked the question. "Why doesn't Mississippi have a Ronald McDonald House?"

As a regional medical center and the only children's hospital in Mississippi, critically ill children from across the state are brought to Jackson each year for hospitalization and treatment. Parents naturally want to be near their children in a time of illness, but living away from home can be tiring, expensive and lonely. The UMC campus was the perfect location for a Ronald McDonald

House. Dr. Blair Batson was chairman of the UMC Department of Pediatrics in the mid 1980's when the grant application was made to the Kroc Foundation.

Dr. Batson, along with other members of the Department of Pediatrics, recognized the need for a facility like the Ronald McDonald House as they treated not only the medical needs of their small patients but also the physical needs of their parents and guardians.

After countless committee meetings, fund drives, contributions, in kind donations, promotions and four years of hard work, the Mississippi Ronald McDonald House opened its doors on April 30, 1989, completely debt free. The project cost 1.2 million dollars.

The Ronald McDonald House provides a warm, friendly, comfortable environment for families at a time when they need it most. According to Dr. Evans, each case and family are special and there are many stories to tell. Dr. Evans said, "many of the stories that stand out are about the families that have come to the hospital with a very sick child, not knowing what they were going to do or how they would live and find that the House is available for their use. Their appreciation makes it all worth-





*Assistant Manger Rosemary Maxey Randle is seen in one of the Ronald McDonald House's nine bedrooms. Additional rooms are planned for the 1994 expansion.*

while."

Families are referred to the House through the social work department at the University Medical Center. The two-story residence has nine comfortable bedrooms with private baths, two fully equipped kitchens where families can prepare their own meals, a large dining room and family room, laundry room, private sitting areas, handicapped facilities and parking area.

The Ronald McDonald House's full-time manager is Ruth Ann Allen. With the assistance of a volunteer support group, she is in charge of the daily House operations and patient-family contact.

Each guest is considered a "temporary volunteer" while residing in the House and is responsible for keeping the facilities in a clean and orderly condition so that other families can also benefit from the Ronald McDonald House.

The cost per family is \$8 a night; but if a family cannot afford it, other arrangements can be made. Through the "Share a Night" program individuals, groups and companies contribute the room cost. The UMC Candlelighters

also contribute support for families of cancer patients.

The House is owned and operated by Lovebilt, Inc., a private non-profit organization. The directors, officers and members are all volunteers. These people see to the governance of and policies under which the House operates. They include parents, medical personnel, business leaders, local McDonald's owners and other individuals who care about the needs of critically ill children and their

families.

Rosemary Maxey Randle, the assistant manager of the House said that many organizations locally and over the state have taken an interest in the Ronald McDonald House and its guests. "Many times we have local groups that come by, bring a meal and just visit with those families staying in the House. We try to make it as much like home as possible."

The Ronald McDonald House needs continued financial support to defray operating expenses and to continue to provide a caring home for families. Plans are underway for an expansion of the facility in the spring of 1994 when a new wing with additional bedrooms will be added.

Families who stay in Mississippi's Ronald McDonald House understand that "Home is where the Heart is."

By their generous contributions, many people have a part of making this House, a very special home for families of critically ill children. □



*One of the fund raising events for the Ronald McDonald House is Northpark Junction, an antique train exhibit now under way at Northpark Mall. Managing the exhibit are, from left: Dell Humphries, Ronald McDonald House Volunteer, Ruth Ann Allen, House Manager and Bob Mathis, Train Society.*



## **The President's Page**

DON Q. MITCHELL, MD

### **Carpe Diem**

**D**ecember is not only a busy month because of the holiday's but also because of the AMA Interim meeting and the MSMA Board of Trustees meeting.

In my travels around the state thus far, as you would expect, there has been a good bit of anxiety and some misgivings expressed about what is going to happen with the anticipated changes in health care. Sometimes it seems that the whole future of medicine is falling apart - giving us reason to despair.

President Clinton has finally submitted "parts" of his plan to the Congress, the Congress has produced several of its own plans, and in Mississippi the Governor's Health Care Commission has issued its recommendations. These plans will be discussed and then discussed over again by all parties involved. One note of encouragement about this process may be found in what Lou Holtz said, "when all is said and done, there is usually more said than done."

Whether Congress or the Mississippi Legislature eventually mandates reform of our Health Care System, or whether we continue to undergo the voluntary, market-driven changes that have already taken place, our state medical association is committed to three fundamental objectives:

1. To create a "Physician" driven and controlled managed care organization within the state, which we have done by establishing the MPCN.
2. To assist the Association's membership in dealing with current and future changes taking place at all levels of our health care system. This includes helping you function better in a managed care environment and under-

*(Continued on page 424)*



## Thanks, Dean Nelson

I first met Dr. Norman Nelson when, as a green third-year medical student, I had the opportunity to scrub with him on a thyroid surgical case. Dr. Nelson was serving his first year as Dean of the University of Mississippi Medical Center, and to say that I was terrified and intimidated at the prospect of working so closely with the new Dean would be an understatement. I remember with clarity both his precise surgical skills and the skills he demonstrated in managing people. He was able to produce a relaxed atmosphere during a tedious surgical procedure, creating an ideal situation for learning. I was impressed then, and I'm still impressed now, some twenty years later.

The past twenty years have seen tremendous growth and progress at UMC in the midst of some of the most difficult times in American med-

ical education, not to mention the health care system in general. Dean Nelson has provided the steady hand on the rudder which guided that progress. He has managed to harness the existing economic and political forces to the advantage of the Medical Center and to the medical community at large. He has indeed been a force for positive change during changing times, and Mississippi has benefited much from his leadership.

Dr. Nelson will be retiring on July 31, 1994, and his successor will have some very large shoes to fill. Thanks, Dean Nelson, for a job well done. You will be fondly remembered, and you will be missed.

**George Abraham, II, MD**  
Associate Editor

The editorial opinions expressed in this Journal are those of the indicated author. Editorial opinions are not expressions of the views, or official policies of The Mississippi State Medical Association. We encourage the membership to submit letters for publication regarding any opinion expressed or information contained in the Journal.

standing the many options and alternatives that are and will be available. We have already sponsored one seminar on this topic and will continue to offer programs on timely health care delivery topics in the future. The MSMA staff can also provide information, advice and consultation on practice matters on an individual basis.

3. Finally, to work closely with our Congressional delegation and the Mississippi Legislature in assuring that whatever changes take place in health care serves the interest of our patients first and fore-

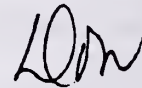
most, and that we have the flexibility to care for our patients in the most appropriate manner.

When you consider these things, the future of medicine is not falling apart. There are opportunities for us to make positive changes in the health care delivery system. Let's not despair, but seize the day and use these opportunities for better health care for all.

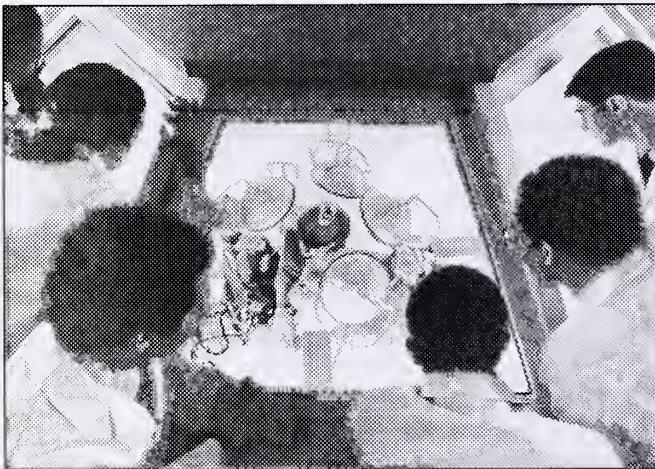
Let us take time this Christmas to remember some of the messages that this season brings -- Hope, Joy, Love, Peace and Goodwill to All Men!

I hope that you and your family are Blessed this holiday season.

Your Colleague:



## **AN ARMY SCHOLARSHIP COULD HELP YOU THROUGH MEDICAL SCHOOL**



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Several months ago, a disgruntled City employee arrived at our clinic and mentioned his anger at not being able to hold a job given a wide variety of bona fide medical problems. He spoke of his desperation, he was feeling helpless and hopeless. In the course of the interview, the patient threatened to return to his former place of employment and kill people. This is not an infrequent occurrence at a mental health clinic and/or, we suspect, at physician's offices generally. It has raised in our minds the question of whether or not one has a duty to warn, and if so, who is to be warned?

There has been substantial legal literature on the subject, it develops. Although there seems to be no case law in the State of Mississippi dealing with the matter, some research that we have performed has raised questions which may be applicable to medical practice in Mississippi.

The gold standard seems to be the case of *Tarasoff v. Regents of the University of California*.<sup>1</sup> While the case is somewhat convoluted, the important features are as follows: a mental health clinic patient killed his fiancée two months after confiding in his psychotherapist that he intended to kill her. When that case came to the California Supreme Court, it was determined that the therapist had a clear duty to warn the intended victim. The criteria seemed to be that a special relationship existed between the patient and his therapist and that the standard of medical practice was such that the therapist could have, or should have been able to determine the dangerousness of the patient in regard to his fiancée. Crucial, in this case, is the fact that the intended victim was named and thus identifiable.

This issue of identifiability existed because the patient had named his fiancée specifically as the intended victim. Thus the therapist was held to be guilty of negligence.

The concept of identifiability was expanded in *Thompson v. County of Alameda*<sup>2</sup> in which a patient indicated that he intended to kill some child in his neighborhood as soon as he was released from the mental hospital. While the specific child was not named, the children who were potentially at risk were clearly identifiable. Again, in *Davis v. Dr. Yong-Oh Lhim*<sup>3</sup> the courts of Michigan ruled that Northville State Hospital was liable when a released mental pa-

tient killed his mother. Although the patient had never mentioned his mother by name, she was readily identifiable since he had expressed his hatred for his mother and his intention to do her harm.

At that time, the Courts indicated that a psychiatrist does not have a duty to warn the public at large, but has a duty to warn a readily identifiable victim.

In an oral communication with legal authorities in the State of Mississippi concerning the *Tarasoff* decision and its progeny, we have been informed that State courts have generally been very supportive of the concept of confidentiality in the doctor-patient relationship. However, it is our contention, that physicians in general may have a moral, if not a legal responsibility to be protective of third parties when they are identifiable. It should also be noted that this matter comes often enough so that it would be appropriate for the medical community to make a statement on this issue.

In situations in which the intended victim is not specifically named, but is generally recognizable (co-workers or supervisors, for example) we have usually notified local law enforcement agencies and have been quite surprised at the lack of awareness on the part of those agencies on procedures for handling such cases. Given the extent of mayhem in the work place and the extent of family violence together with the ready availability of weapons we wonder if it would not be appropriate for the membership to make known its opinion in the matter.

**Murray Feldberg, MD**  
Region VI MH-MR Center  
Greenwood, MS

Appreciation is expressed to Joseph Downing, Executive Director for his kind support of this research activity.

1. *Tarasoff v. Regents of California*, 17 Cal.3d 425, 131 Cal. Rptr. 14, 551 p. 2d 334 (Cal. 1976)
2. *Thompson v. County of Alameda*, 27 Cal. 3d 741, 167 Cal. Rptr. 70, 614 p. 2d 728 (1980)
3. *Davis v. Dr. Yong-Oh Lhim*, 124 Mich. App. 291, 335 N.W. 2d 481 Docket No. 59284 (3-21, 1983)



**Seasons Greetings and Best Wishes for a  
Healthy and Prosperous New Year**  
from the

**MSMA Alliance Officers and Board on behalf of the AMA-ERF**

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Roberta Barnett  
Nancy Bush  
Kathy Carmichael  
Peggy Crawford  
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Sylvia Walker  
Barbara Webb  
Martha Whitehead  
Merrie Wiley

The Christmas Card featured above is taken from a painting by Edsel F. Stewart. Dr. Stewart, an obstetrician-gynecologist and artist, has achieved remarkable success in both fields. Dr. Stewart received his medical degree from the University of Virginia. At age 50, he returned to college, earning a master's degree with honors in studio art. Dr. Stewart's work is in many private and corporate collections. He has won numerous awards in local and state shows, including the American Physicians Art Association, of which he is immediate past president.

The Card is available for sale through the MSMA Alliance as a fund raising effort for AMA-ERF. Contact your local Alliance for further information.



## American College of Surgeons MS Chapter Holds Fall Clinical Meeting

The Mississippi Chapter of the American College of Surgeons held its Fall Clinical Meeting, November 19-20 in Jackson.

The meeting was held in conjunction with the ACS Region IV Resident's Research Competition and The Cancer Liaison of the Mississippi ACS Chapter.

Over 100 physicians, spouses and guests attended the Friday evening reception and dinner. Guest speaker for the occasion was Dr. John Tarpley. Dr. Tarpley, a medical missionary in Nigeria for most of the past fifteen years, provided the audience an interesting evening by describing the practice of surgery in the tropics and telling about his life as a medical missionary.

The ACS Chapter clinical meeting, which began on Saturday morning, was divided into three sections: Current Topics in Cancer Surgery, Selected Topics in Laparoscopic Surgery and General Surgical Topics with chapter members presenting information on each topic. Chapter members also had the opportunity to hear the residents' papers presented during the Trauma Research Paper Competition. More than 75 physicians attended the Saturday session.

Current officers of the MS Chapter are: President Charles S. O' Mara, MD, Jackson; President-elect John F. Lucas, Jr., MD, Greenwood and Secretary/treasurer Ralph H. Didlake, MD, Jackson. □



*MS Chapter ACS 1993-94 officers are: from left, Ralph H. Didlake, MD, secretary-treasurer; Charles S. O'Mara, MD, president and John F. Lucas, Jr., MD, president-elect.*



*Attending the ACS Chapter meeting were, from left: Richard J. Field, Jr, MD, Regent and Second Vice-president elect of the American College of Surgeons; Raymond Martin, MD and his wife Margery.*

## **Dr. Field Elected ACS Second Vice President**

Dr. Richard J. Field, Jr., of the Field Clinic and the Field Memorial Community Hospital of Centreville, was elected second vice president-elect of the American College of Surgeons at their annual clinical congress in San Francisco in October.

Dr. Field has just completed his

position as regent of the American College of Surgeons, a position he has held since 1984.

The American College of Surgeons was founded in 1913 with its major endeavor begin to improve the quality of care to surgical patients. In addition it has been a world leader in standardization of

operating rooms, hospitals and ambulance services. It is the largest surgical organization in the world extending throughout North and South America and into twenty-three foreign countries. There are fifty-five thousand members at the present time.

Dr. Field will take office as second vice president at the Clinical Congress which will be held in New Orleans in October of 1994. □

## **Dr. McMullan Receives Prestigious Mississippi College Award**

Mississippi College honored Dr. Martin H. McMullan, a Forest native, with the prestigious "Order of the Golden Arrow" award, recognizing him for dedication to the College and his professional achievement in his chosen profession. Dr. McMullan is a cardiovascular surgeon practicing in Jackson.

The presentation was made during the annual Alumni Luncheon on Homecoming Day. The award is one of the highest given by the National Alumni Association and is reserved for those alumni and friends who have displayed loyalty to the institution and excelled in their particular area of service.

Dr. McMullan received his bachelor of science degree from Mississippi College in 1962, serving as president of the Student Body Association his senior year and elected to Omicron Delta Kappa. He was a standout player on the Choc football team, with the '61 team going 8-1 and McMullan captured the Sportsman Trophy.

Following his graduation from MC, he entered the University of Mississippi School of Medicine and was awarded the doctor of medicine degree in 1966. He did his mixed surgery internship and general surgery residency at the Mayo Clinic in Rochester, MN.

Dr. McMullan is associated with

the Cardiovascular Surgical Clinic, P.A., in Jackson and since 1988 has held an academic appointment at the University of Mississippi School of Medicine as clinical assistant professor of surgery and visiting teaching physician. He holds certification by the American Board of Surgery and the American Board of Thoracic Surgery.

He is a member of numerous professional medical associations and societies and active in the American and Hinds County Heart Associations. He is a member of the staff and former president of the staff of Mississippi Baptist Medical Center. He is a consulting member of the staffs of St. Dominic-Jackson Memorial Hospital, Rankin General Hospital, River Oaks Hospital and Methodist Medical Center. □

## **Dr. McIlwain Elected to AMPRA Executive Committee**

Dr. James S. McIlwain, Medical Director for the Mississippi Foundation for Medical Care, Inc., has been elected to the Executive Committee of the Medical Director's Section of the American Medical Peer Review Association (AMPRA). AMPRA is a national membership

association and network of state-based independent quality improvement organizations. AMPRA is dedicated to improving the quality of health care for all consumers through creative application of quality evaluation and consumer protection programs and services.

AMPRA's current membership includes the federally designated peer review organizations (PROs) under contract with the Medicare program. The Mississippi Foundation for Medical Care, Inc. is the Peer Review Organization (PRO) for the state of Mississippi. □



## Brothers To Share Alumnus Award At Mississippi College

For the first time in history, brothers will share the Mississippi College Alumnus of the Year award.

The presentation was a highlight of the MC homecoming held in the A. E. Wood Coliseum, the building that carries the name of their late father.

Dr. James P. Wood of Waynesboro, class of 1941, along with his brother, Dr. Arthur E. Wood, Jr., of Inverness, class of 1947, were honored by the National Alumni Association with its highest honor.

Both medical doctors, they either gave or assisted in raising in excess of \$500,000 for the construction of the A. E. Wood Coliseum, one of the most utilized buildings on the MC campus.

Their dad served as professor and head of the Department of Chemistry for many years, developing the department into one of the finest in the South. He was

also a longtime mayor of the city of Clinton.

Both brothers received Service to Humanity Awards from the College in 1976, the sesquicentennial year, and both have been loyal supporters through the years and active in alumni activities.

Dr. James Wood received the bachelor of arts degree from Mississippi College in 1941 and served in the Armed Forces of the United States for three years during World War II. He entered the Tulane University School of Medicine in 1946 and earned the doctor of medicine degree in 1950. He served as an intern at Charity Hospital in New Orleans for a year before establishing a family practice in Waynesboro.

He has been active in numerous medical organizations and civic groups. He has also served on the Mississippi State Oil and Gas Board and the Mississippi Energy and

Transportation Board and is a former member of the Green County Board of Education.

Dr. Authur Wood, Jr. is a double graduate of Mississippi College. He earned the bachelor of science degree in 1947 and in 1963 was awarded the bachelor of laws degree from the Jackson School of Law, forerunner to the Mississippi College School of Law. He completed his law degree by attending school at night.

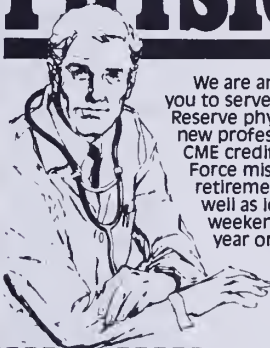
In between those degrees, he attended Tulane University School of Medicine in New Orleans, receiving the doctor of medicine degree in 1953. He has been a practicing family physician since.

A veteran of the U.S. Navy during World War II, he holds membership in many medical societies, including the American Medical Association, the Mississippi State Medical Association, the American Academy of Family Physicians and the Mississippi Academy of Family Practitioners. He is also a member of the Mississippi State Bar Association. □

## MAFP Members Appointed

The Mississippi Chapter of the American Academy of Family Physicians (AAFP) received notice that several MAFP active members have been appointed to the 1994 AAFP Commission and committee membership. Dr. Stanley Hartness of Kosciusko was appointed to the Committee on Bylaws and Dr. Susan Chiarito of Vicksburg was appointed resident representative to the Committee on Health Education. Dr. Eugene Wood of Jackson continues to serve on the Commission on Membership and Member Services. Appointments to Committees are for a one-year term and Commission appointments are for a period of three years. □

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## MSMA Alliance Holds Legislative Rally



United States Senate, Washington, DC 20510 and The Honorable \_\_\_\_\_, United States House of Representatives, Washington, DC 20515.

As the spouse of a physician and a member of the Alliance, your support, your voice, and your dedication to the health of all Americans is of utmost importance. Be involved!

**Nancy Lindstrom,**  
Alliance Representative  
MSMA Council on Legislation

MSMA Alliance members from over the state were both informed and challenged at the Legislative Rally held in Jackson, on Wednesday, November 10, at the Mississippi Museum of Art. MSMA Director of Legislative Activities Clare Hester, prepared the Alliance for the 1994 legislative session; and Liz Kagan, AMA Alliance Legislative Affairs committee members from Fort Meyers, Florida, analyzed the Clinton Health Reform plan.

The need for medicine to be truly organized and unified has never been more urgent. We support health system reform, but have serious reservations about the President's plan as it would limit choices by patients and physicians, undermine the quality of medical services, and lead to federal control of medical education and physician work force. The President's plan, however, will not be enacted as proposed. This is the beginning of a long national debate, and Alliance members must work closely with the medical association to meet medicine's goals in both state and national health care reform.

Alliance members should also:

1. Be informed - Read the analysis of the AMA response mailed to all physicians, and then stay informed via AMA News, current TV, newspaper, and magazine reports.
2. Share AMA's message with patients - The AMA has produced a brochure, "How Will The Clinton Reform Proposal Affect You and Your Family?" Call 1-800-262-3211 for copies.
3. Communicate Medicine's Viewpoint on Health System Reform - Launch a "letter to the editor" campaign, participate in radio call-in or talk shows, and/or develop a "speakers' bureau" of informed physicians and alliance members to speak to local civic clubs and other community groups.
4. Write to your legislators - The Honorable \_\_\_\_\_,



*Nell Middleton, Chairman MSMA Alliance Legislative Affairs Committee, served as meeting chairman.*



## UMC Receives \$6 Million Grant For Cardiovascular Study

The Department of Physiology and Biophysics at the University of Mississippi Medical Center has received a \$6.8 million grant to study heart and blood vessel physiology.

Twenty-seven members of the department participate in the project funded by the National Institutes of Health (NIH). Each works on one of six research programs which contribute to the total project, "Cardiovascular Dynamics and Their Control."

Dr. John Hall, chairman of the department, is principal investigator.

The project, funded since 1969, has already brought more than \$25 million to Mississippi and the Medical Center.

The grant reviewers called the proposal "outstanding," and assigned it a priority score of 120, making it rank in the top 1.9 percent of all NIH grant applications for merit.

Since its inception, the project has resulted in "several fundamental contributions to the understanding of long-term control of the circulation," the reviewers noted, and "more than 1,800 publications in science journals."

Dr. Hall, who succeeded Dr. Arthur Guyton as department chairman and principal investigator, says the project also has trained "an entire generation of systems physiologists." Some 25 of the department's graduates are physiology department chairs around the

world, including Dr. Hall.

Ultimately, the project will yield the answer to the cause of hypertension or high blood pressure, the world's major health problem which can lead to stroke, heart attack, and maternal and fetal death. Although hypertension is treatable in most instances, and UMC physiologists have narrowed the focus of cause to the kidneys, much remains to be known about how kidney dysfunction brings about a rise in pressure.

"The obvious questions is, why are we still being funding if we haven't managed to solve the problem in 25 years," Dr. Hall says.

"The answer is that clinical hypertension is for more complex than our original naive belief. And we also discovered a paucity of information about basic cardiovascular and kidney function. We had to discover the basics before we could even begin to think about looking for the many different causes of hypertension," Dr. Hall said.

The research program is rare in its ability to observe long-term changes in blood pressure. "You have to see the effects of any interventions, not overnight or for two or three days, but for weeks and months.

The project was one of the first to use computer simulations of biological functions.

"The computer doesn't take the place of animal research. Computer programs are used to predict new

concepts and to help design experiments. In turn, the lab work tests the concepts and provides data which make the computer model more comprehensive, more helpful," Dr. Hall said. □

## Dr. Long Receives Hofman Award

Dr. William A. Long, Jr., clinical associate professor of pediatrics at the University of Mississippi Medical Center (UMC), has been named recipient of the Adele Dellenbaugh Hofmann Award.

The award is given by the Section on Adolescent Health of the American Academy of Pediatrics (AAP) for "exemplary achievement in the field of adolescent health."

As advocate for the nation's teenagers, Dr. Long served on the AAP's Committee on Adolescence for several years and then as its chairperson from 1980-1983. He was a charter member of the Section on Adolescent Health, served on the executive committee and was section chairperson for 1986-1988.

Dr. Long joined the UMC faculty in 1969. □

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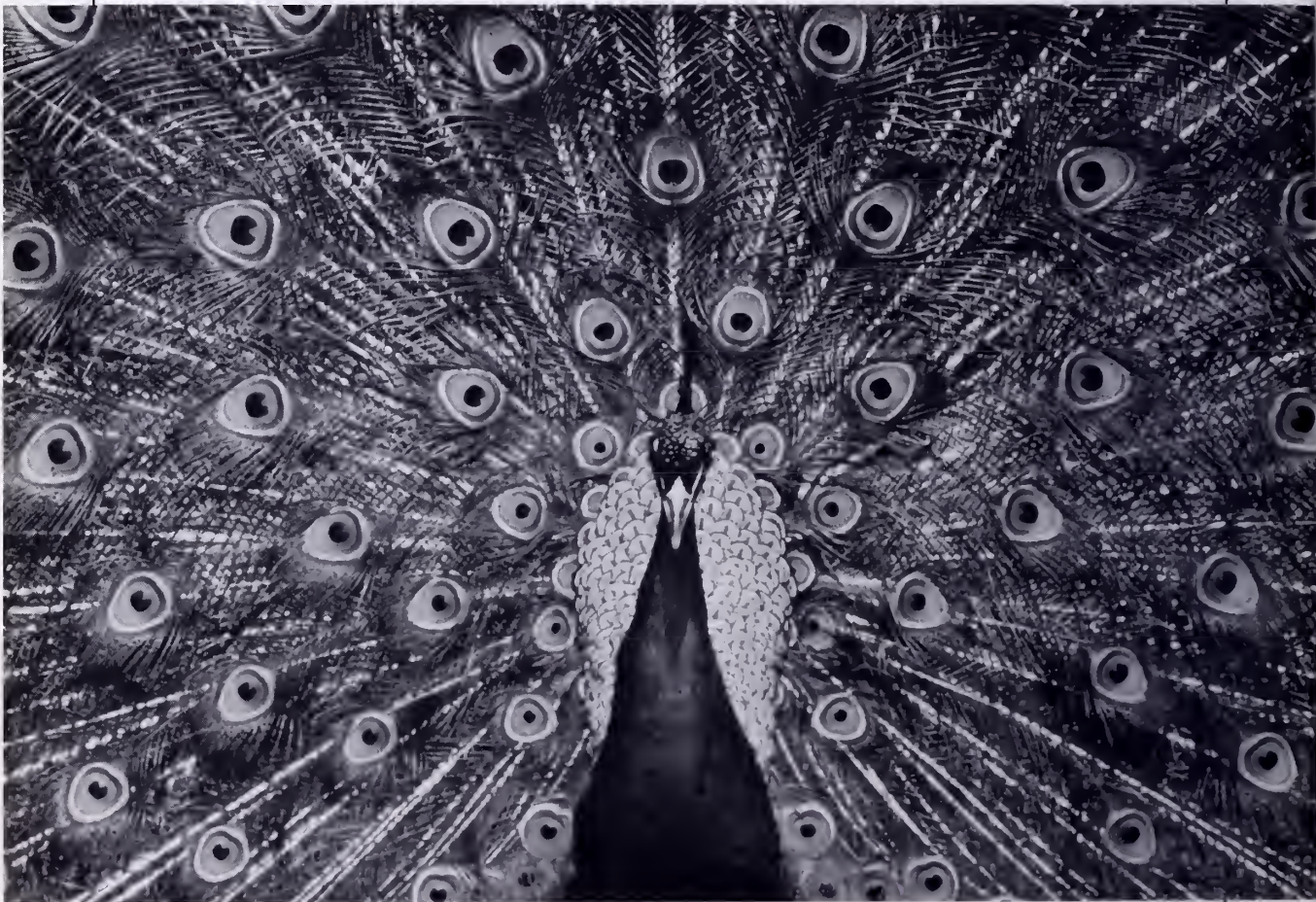
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# New Members

**Azordegan, Phillip A.**, Jackson. Born Jackson, MS, April 6, 1961; MD, Johns Hopkins, Baltimore, MD, 1987; surgery & neurosurgery residency Baylor College of Medicine, Houston, TX, 1987-93; elected by Central Medical Society.

**Bowden, Douglas E.**, Greenwood. Born Tulsa, OK, January 23, 1961; DO, University of Oklahoma College of Osteopathic Medicine, Tulsa, OK, 1987; internship and surgery residency, Tulsa Regional Medical Center, Tulsa, OK, 1987-92; elected by Delta Medical Society.

**Bullock, John David**, Hattiesburg. Born Hattiesburg, MS, November 2, 1956; MD, University of Mississippi School of Medicine, Jackson, MS, 1988; family practice residency, University of Alabama at Tuscaloosa, Tuscaloosa, AL, 1988-91; elected by South Mississippi Medical Society.

**DeLima, Luiz G. R.**, Jackson. Born Brazil, August 31, 1949; MD, School of Medical Science of the University of Rio de Janeiro, Brazil 1974; anesthesiology residency University of Washington, Seattle, WA, 1988-91; fellowship in cardiac anesthesia and research, University of Ottawa Health Institute, Canada, 1991-93; elected by Central Medical Society.

**Eluson, Parker L.**, Jackson. Born San Francisco, CA, October 13, 1964; MD, University of Mississippi School of Medicine, Jackson, MS, 1990; residency in pediatrics, Vanderbilt University School of Medicine, Vanderbilt Hospital, Nashville, TN, 1990-93; elected by Central Medical Society.

**Fletcher, Gardner L.**, Hattiesburg. Born Shirley, MA, July 15, 1956; MD, University of Mississippi School of Medicine, Jackson, MS, 1982; residency in internal medicine, Beaumont Army Medical Center, El Paso, TX, 1982-85; fellowship in pulmonary and critical care, Walter Reed Army Medical Center, Washington, DC, 1987-89; elected by South Mississippi Medical Society.

**Hutchens, Dennis W.**, Jackson. Born Ashland, AL, August 25, 1963; MD, University of South Alabama College of Medicine, Mobile, AL, 1989; interned one

year Marshall University affiliated hospital, Huntington, WV; anesthesiology residency, University Medical Center, Jackson, MS, 1990-93; elected by Central Medical Society.

**King, Coleman T.**, Jackson. Born Rome, GA, June 1, 1957; MD, Medical College of Georgia, Augusta, GA, 1985; interned one year, Tulane Hospital, New Orleans, LA; internal medicine residency, University of South Florida, Tampa, FL, 1986-88; fellowship in infectious disease, University Medical Center, Jackson, MS, 1989-91; elected by Central Medical Society.

**Scharf, Steven M.**, Jackson. Born Philadelphia, PA, December 7, 1960; DO, Philadelphia College of Osteopathic Medicine, Philadelphia, PA, 1987; anesthesiology residency, Farmington Hills, MI, 1988-91; elected by Central Medical Society.

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**Paul M. Allen**, a gynecologist and obstetrician practicing in Pascagoula, gave a presentation entitled *Howard Atwood Kelly, MD (1858-1943) His Life and Enduring Legacy* at the University of South Alabama, Department of Obstetrics and Gynecology, Grand Rounds Conference in October and at the Depart. of OB/GYN, Grand Rounds Conference at Mount Sinai Hospital in Hartford, CT, in November. Dr. Kelly was influential in development of the specialty of gynecology approximately 100 years ago and was one of the founders of the Johns Hopkins Hospital and School of Medicine in Baltimore, MD.

**C. Ron Cannon** of Jackson has been asked to serve as the new chairman of the Nominee Platform Committee of the American Academy of Otolaryngology-Head and Neck Surgery, Inc.

**Kenneth Gaines** has associated with Baptist Memorial Hospital - North Mississippi in the practice of neurology, 2301 South Lamar, Oxford.

**Eugene Hesdorffer** of Jackson is not retired as listed in the MSMA Membership Directory, His office is located at 971 Lakeland, Dr., Ste 554, Jackson, MS 39216-4607.

**J. Edward Hill** of Hollandale has been elected vice president of the Southern Medical Association for 1994.

**Coleman King** has associated with Infectious Diseases Associates of Jackson for the practice of infectious diseases medicine, 768 Lakeland Drive, Jackson.

**Ben Kitchings** of Long Beach was recognized for 32 years of continued membership in the American Academy of Family Physicians at the group's 45th annual Scientific Assembly in Orlando, FL.

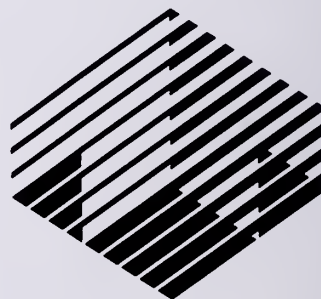
**Zina Darcell Lee** has joined the staff at South West Mississippi Regional Medical Center, McComb in the practice of internal medicine.

**William A. Middleton** of Winona has completed continuing medical education requirements to retain active membership in the American Academy of Family Physicians (AAFP).

**R. Keith Partridge** has associated with the Wiggins Clinic, a satellite facility of Hattiesburg Clinic, in the practice of Family Medicine.

**Daniel J. Peasley** announces the opening and relocation of his medical practice, The Gastroenterology Clinic, to 1020 Adams Street, Laurel.

**Felix Savole** of Jackson was an instructor at the Arthroscopy Association of North America Fall Course on Arthroscopy of the Shoulder and Arthroscopy of the Wrist in Albuquerque, New Mexico during October. He was also a featured lecturer at the 5th Congress of the Sociedad Venezolana de Cirugia de la Mano in Valencia Venezuela where he made presentations of arthroscopy and reconstruction of the shoulder, arthroscopic and open procedures of the elbow and arthroscopy and reconstruction of disorder of the wrist.



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## Physicians' Recognition Award



Four MSMA members were named recipients of the AMA Physicians Recognition Award in October 1993. This award is presented by the American Medical Association to Physicians who have voluntarily completed a specified number of continuing medical education hours. These individuals are presented below by Medical Society.

**DELTA MEDICAL SOCIETY**  
**John Phenis Hey, MD**

**NORTHEAST MISSISSIPPI MEDICAL SOCIETY**  
**Linda Fay Chidester, MD**

**SINGING RIVER MEDICAL SOCIETY**  
**Jeff Allen Hodges, MD**

**WEST MISSISSIPPI MEDICAL SOCIETY**  
**Walter E. Johnston, MD**

Applications for the AMA Physicians Recognition award can be obtained at any time by writing or calling the AMA Office of Physician Credentials and Qualifications: (312) 464-4672.

**Robin H. Schwartz** has associated with Anesthesia Consultants for the practice of anesthesiology, 1640 Lelia Drive, Suite 120, Jackson.

**James C. Waltes**, of Laurel has been selected as Southern Medical Association's State Councilor from Mississippi during the SMA's 87th Annual Scientific Assembly recently held in New Orleans.

**Jo P. Wilson**, of Jackson recently attended the Interscience Conference on Antimicrobial Agents and Chemotherapeutics held in New Orleans, LA.

**Joseph Bingham Witty, Jr.**, of Columbus has been recertified by the American Board of Obstetrics and Gynecology Inc. □



"Ron's Rule—I give myself one week to meet new people and start having fun on a locum tenens assignment. It hasn't failed me yet."

Ron Richmond, MD, joined the CompHealth locum tenens medical staff when he completed his residency. He wanted to travel. He loves to meet people.

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practice medicine

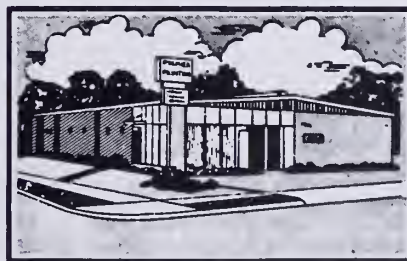
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# INDEX

## VOLUME XXXIV

January - December 1993

### SUBJECT INDEX

The letters used to explain in which department the matter indexed appears are as follows: "A," Abstract; "E," Editorial; "N," News; "L," Letters to the Editor; "PP," President's Page; "RS," Radiologic Seminar; "BR," Book Review, "ME," Medical Ethics; "AP," Auxiliary Page; "C," Comments; "S," Special Article; the asterisk (\*) indicates an original article in the Journal, and the author's name follows the entry in brackets. "Deaths," "Personals," and "New Members" are indexed under the letters "D," "P," and "M," respectively. Matter pertaining to MSMA is indexed under "Mississippi State Medical Association."

#### A

##### ACS

American College of Surgeons, Mississippi  
Chapter Fall Clinical meeting: abstracts for  
presentation, \*335

##### AMA

1993 annual meeting of the AMA House of  
Delegates, 269-S  
delegates report - 1992 AMA interim meeting  
of the House of Delegates, 11-S

##### AMA physicians recognition award

Allen, Clyde R., 136  
Alexander, J. Gilbert, 171  
Alexander, Richmond L., 217  
Ball, David Kyle, 294  
Britton, Albert B., 217  
Burris, Richard G., 217  
Chidester, Linda Fay, 435  
Clark, Cheryl Gay, 217  
Coghland, Robert E., 217  
Collins, Robert Keith, 30  
Daniel, C. Ralph, III, 136  
Doyle, Donald Edward, 406  
Ervin, James W., 217  
Fly, James Douglas, 30  
Forks, Thomas Paul, 406  
Gabbert, Elmo P., 67  
Gorman, Douglas E., 171  
Groff, Gary H., 217  
Harris, Joe Mark, 217  
Henson, L. C., 217  
Hey, John Phenix, 435  
Hodges, Jeff Allen, 435  
Holmes, James W., 67  
Horowitz, Michael D., 294  
Isbell, Jimmy E., 100  
Jett, Pamela, 217  
Johnston, Walter E., 435  
Keel, Daniel T., Jr., 67  
Lambert, Stephen C., 217  
Lay, Adron Keith, 406  
Liberto, Vincent, 217  
Lott, Chester C., 294  
McDonnell, Fred J., 217

Mestayer, Roland Joseph, 406

Patel, Pravinchandra P., 67

Pritchard, D. Alan, 217

Reyes, Cirila L., 67

Rhoden, Richard E., 136

Robinson, Joseph H., 67

Scott-Conner, Carol E. H., 406

Temple, William Meredith, 406

Tilton, Frank McVey, 294

Undesser, Cynthia L., 217

Warrington, James E., 171

White, Elbert A., 100

Woods, Eugene G., 406

Wyble, Eric J., 136

##### Androgen Insensitivity Syndrome

testicular vein and peripheral vein testoster-  
one, follicle stimulating hormone,  
luteinizing hormone, and prolactin  
concentrations in a patient with androgen  
insensitivity syndrome, [Meeks, et al]  
\*263

##### Aplastic Crisis

aplastic crisis due to human parvovirus (B19)  
as an initial presentation of hereditary  
spherocytosis, [Megason, et al] \*107

##### Arterial Injury

unpected arterial injury, [Bross & Stefani]  
\*42

##### Arthroplasty

total elbow arthroplasty: salvage of  
unsuccessful previous elbow surgery,  
[Savoie] \*259

#### C

##### Cancer

evaluation of mammographic stellate lesions  
[Flowers and Powers] \*7

#### D

##### Deaths

Bise, John R., III, 326  
Buck, William H., 403  
Campbell, Guy D., 66  
Cook, Wendell H., 326

Crull, Luther P., 134

Ellis, Donald R., 212

Farber, Louis A., 66

McBryde, Angus M., 212

Mitchell, J. Dan, 66

Parker, W. H., 66

Stephenson, Samuel L., 251

Turnage, John Neil, 66

Tyler, Charles C., 134

Williams, J. Collins, 212

#### E

##### Elbow

total elbow arthroplasty: salvage of  
unsuccessful previous elbow surgery,  
[Savoie] \*259

#### H

##### Health Reform

"details, details", [England] 335-E  
overall physician cost effectiveness,  
[Abraham] 193-E  
physicians invited to discuss administration's  
reform plan, [Hill] 195-C  
the new PRO, [Cobb] 389-S  
you know the plan is in trouble when she  
comes to the AMA, [England] 239-E  
waiting for the windfall, [Lockey] 121-E

##### Home Health

home health reimbursement, [Abraham] 87-  
E

##### Hospice

Hospice care, [Duddlestone, Edwards] 233-S

#### L

##### Laparoscopy

laparoscopic colectomy for sigmoid  
volvulus, [Pruett] \*73  
laparoscopic inguinal herniorrhaphy: initial  
experience in a community hospital,  
[Pruett] \*377

##### Letters

Comments, [McIlwain] 395-C; [Feldburg]  
425-C  
to the Editors, [Morris] 17-L; [Currier] 397-L



to MSMA, [Saccocia] 157-L; [Cobb] 240-L;

## M

### Malpractice

the effects of malpractice on Mississippi physicians, [Polles and Neral] \*77

### Managed Care

vertical integration, clinic without walls, physicians-hospital organizations: what it means and is it right for you?, 411-S

### Medical Ethics

current opinions on practice matters, 19-ME; current opinions on professional rights and responsibilities, 93-ME, 123-ME

### Medical Licensure Board

Mississippi State Board of Medical Licensure Annual Report July 1, 1991 through June 30, 1992 [Morgan] 46-S

### Medical Organization

125th annual session, 115-S

125th annual session highlights, 198-N

actions of the House of Delegates 125th

annual session April 28 - May 2, 1993, 200-N

address of the president, [Gates] 187-S

Biloxi MSMA 1993: a meeting in review, [South] 241-C

brothers to share alumnus award at Mississippi College, 429-N

Dr. Lee appointed to risk pool association board, 162-N

elected officers, board and council members, 199-N

letter to God, [Johnson] 56-E

Mississippi physicians participate in national

coalition against family violence, 161-N

MSMA 125th Annual Session program overview, 98-N

MSMA resolution calls for increasing drivers license age, [Lockey] 393-E

new charity immunity law, 235-S

over 1,100 Mississippi students attend Health Choice 93, 164-N

women in medicine, 306-S

### Medical Organization News

1993 Caldwell award winner, 246-N

AAP Chapter receives recognition, 365-N

American College of Surgeons Ms Chapter holds Fall Clinical meeting, 427-N

Carthage physician elected president of the MAFP, 361-N

Dr. Authur Aaron Drick, Jr., MSMA past president dies, 127-N

Dr. C. D. Taylor, a long time coast physician dies, 126-N

Dr. Cobb honored by Multiple Sclerosis Society, 365-N

Dr. Cobb retires after almost 20 years as state health officer, 21-N

Dr. Ed Thompson appointed interim State Health Officer, 59-N

Dr. Fenter receives first A. A. Derrick memorial award, 245-N

Dr. Field elected ACS Second Vice President, 428-N

Dr. Field installed as Surgical Congress President, 246-N

Dr. George Abraham presents workshop on patient education, 22-N

Dr. Hollis serves as president of the American College of Obstetricians and Gynecologists, 245-N

Dr. John McGraw elected president of Medical-Dental Fellowship, 22-N

Dr. McDonald guest lecturer, 244-N

Dr. McIlwain elected to AMPRA executive committee, 428-N

Dr. McMullan receives prestigious Mississippi College award, 428-N

Dr. Pharr recognized at goodwill salute, 364-N

Dr. Stockton honored for health, welfare ministry, 243-N

Dr. Ward is new medical examiner, 281-N

Dr. Webb chosen family physician of the year by Mississippi Academy, 360-N executive officer recipient of federation award, 247-N

governor's commission on health care holds final public hearing in Jackson, 321-N

Hattiesburg project wins national health award, 288-N

Kirk Mullins of Natchez receives Evers and Tolbert awards, 244-N

MAFP members appointed, 429-N

medical society gives local students awards for academic excellence, 246-N

Mississippi Children's Immunization Awareness Project, 318-N

Mississippi Thoracic Society honors Dr. Guy Campbell at annual meeting, 400-N

MSMA Alliance holds legislative rally, 430-N

MSMA Board holds summer meeting, 319-N

MSMA Board of Trustees and offers meet, 23-N

MSMA 1993 Socio-economic and legislative forum held January 19th in Jackson, 60-N

MSMA sponsors managed care workshop for physicians, 399-N

Pizza lunch for 1st and 2nd year med students, 362-N

scholarship endowment honors Dr. W. H. Parker, 281-N

seven Mississippi physicians appointed cancer liaisons, 282-N

Thad Waites, MD installed as president of the AHA Mississippi affiliate, 360-N

the 2nd annual Mississippi State Coalition Against Domestic Violence Conference, family violence and sexual assault: the health care response was held August 26-27 in Jackson

### Medical Practice

a doctor's adventure in motherland, [South] 315-C

affordable health care, [Dabney] 278-E

back then - plus ten commandments for graduates with illustrative cases, [Hardy] \*83

doctor, why do you make so much? [Mitchell] 392-PP

Hippocrates revisited, [Abraham] 313-E medicine in 1993, [Lockey] 15-E;

on appreciating patients, [South] 157-L

the walt principle, [Mitchell] 154-PP

same song: last verse [Johnston] 155-E

### Medicine

clinicopathologic conference I, [Files] \*111

clinicopathologic conference II, [Files] \*227

clinicopathologic conference III, [Files] \*346 physicochemical stress in the production of

disease, [Furr] \*382

### Members, New

Alemar, Gilberto Orlando, 324

Azordegan, Phillip A., 433

Barbee, W. Ralph, 133

Barton, Jeffrey Scott, 324

Bernado, Kerry L., 324

Bertolet, Toni J., 330

Bianco, Anthony C., 64

Bolton, Gary G., 324

Booth, Patrick K., 324

Bowden, Douglas E., 433

Brawner, William C., 324

Bullock, John David, 433

Campbell, Jonathan C., III, 324

Casano, Peter J., IV, 251

Cemelicek, John T., 64

Chain, Jeffrey R., 324

Collins, Curtis L., 403

Cook, John W., 324

Coss, Pacita R., 403

Crompton, John D., 133

Davis, Ronald D., 210

DeLima, Luiz G. R., 433

Derbes, Lawrence J., Jr., 210

Doorenbos, David I., 133

Dungan, V. Craig, 324

Eluson, Parker L., 433

Feldberg, Murray S., 251

Fidei, Frank G., 324

Flanagan, Karen Ann, 210

Fontaine, David, 324

Forks, Thomas P., 324

Friloux, Mark A., 210

Gilliland, David H., 210

Horowitz, Michael D., 133

House, James R., III, 403

Hutchens, Dennis W., 433

Jarmon, Henry M., Jr., 325

Jenkins, Ronald A., 64

Jimenez-Agosto, Jamie, 64

Johnson, Jeffery A., 64

Jones, Dan, 133

Kanosky, Michael Glenn, 251

King, Coleman T., 433

Kumar, Vinay, 64

Lee, Zina D., 403

Lenox, Valerie R., 210

Lowe, Terry R., 325

Lundy, McKinley S., 325

Maddux, Robert F., 325

Mallette, Presley D., 251

McKenzie, Antonette L., 65

McKibben, Everett C., 133

Mills, Thomas P., 325

Moman, Maria M., 210

Nelson, Scott E., 65

Newell, Ronald B., 251

Nicholas, Lawrence M., 251

Nix, R. L., 133

Partridge, R. Keith, 325

Payne, Patricia A., 212

Powell, Rhonda H., 326

Psikogios, Michael L., 212  
 Reed, William Ray, Jr., 403  
 Rigsby, Reginald D., 65  
 Rogers, Clifton, 251  
 Ryan, Hewitt Fitts, 251  
 Searcy, Edwin E., 326  
 Seicshnaydre, Michael A., 326  
 Shah, Nikhil S., 403  
 Sharp, Richard B., 326  
 Shields, Roderick A., 326  
 Soucie, Pierre F., 134  
 Stanford, J. Keith, 251  
 Stefani, Anne M., 134  
 Stogner, Steven W., 134  
 Stokes, J. Michael, 134  
 Tabataball, Ashraf, 212  
 Thomae, Keith R., 326  
 Thompson, Anne R., 134  
 Tiwari, S. C., 326  
 Turner, Gerald Alan, 403  
 Vaughn, Cynthia Ann, 251  
 Wallen, Reginald Mark, 326  
 Weber, Benjamin M., 326  
 White, Clinton B., 65  
 Willis, Jeffery Todd, 326, 403  
 Willis, Walter L., 65  
 Woody, Walter W., 326  
 Young, W. Daniel, 134

## O

### Obstetrics and Gynecology

maternal mortality in Mississippi, [Moore, et al]\*35

an assessment of obstetric services in Mississippi [Copeland, et al]\*143

### Orthopaedics

slipped capital femoral epiphysis, a problem of diagnosis [Kendig, Field and Fisher]\*147

## P

### Personals

Abangan, Roland T., 217  
 Acosta, Joseph Robert, 328  
 Adams, Thomas, 135  
 Adkins, Todd N., 214  
 Alford, Tim, 253  
 Allen, Cynthia E., 68  
 Allen, Paul M., 100, 253, 405, 434  
 Alexander, Richmond, Jr., 169  
 Anderson, William E., 68  
 Andy, Orlando J., Jr., 293  
 Archer, Noah, 328  
 Arnett, William, 253  
 Avara, William T., III, 67  
 Bailey, Robert E., 405  
 Ballentine, Michael Stuart, 100  
 Barksdale, Bryan, 214  
 Barton, Jeffery S., 328  
 Barrett, J. Patrick, 369  
 Benefield, Donald W., 67  
 Benson, Chris H., 294  
 Boone, Walter T., 294  
 Borrell, Luis V., 253  
 Bradford, Nathan F., 369  
 Brand, Woodrow W., III, 293  
 Brawner, William C., 293  
 Breeland, Donna G., 136  
 Brisenio, O. J., 100, 253

Brown, James L., 328  
 Burnett, Walter, 214  
 Burris, Richard Gerald, 169  
 Bush, Freda McKissic, 136  
 Bush, William G., 135  
 Butler, Harry, 293  
 Buttross, Susan, 293  
 Calcote, Robert W., 293  
 Callender, William Ray, Jr., 328  
 Cannon, C. Ron, 100, 214, 328, 434  
 Carney, P. Temple, 67  
 Carlton, Rick, 253  
 Carr, Gary D., 369  
 Carter, William Larkin, III, 293  
 Cartwright, Clifton C., 28  
 Chain, Jeffery R., 369  
 Chance, Rickey, 214  
 Chandler, Lisa Leigh, 328  
 Chidester, Linda, 253  
 Chism, Jimmy R., 67  
 Clay, John C., 369  
 Cobb, Alton, 369  
 Coffey, John, 328  
 Cole, Craig A., 28  
 Collins, Curtis L., 328  
 Collins, Robert K., 214  
 Coltharp, J. Robert, 215  
 Conerly, Donald V., 28  
 Cook, John, 253  
 Cook, John W., 293  
 Cooke, Maxwell, C., 67  
 Cosby, Walter N., 169  
 Crosby, Samuel, 67, 215, 328  
 Coss, Pacita R., 369  
 Cunningham, Richard J., 67  
 Curry, Robert Hugh, 328  
 Daniel, C. Ralph, III, 100, 253  
 Davis, Gary, 215  
 Davis, Kenneth M., 28  
 Derbes, Lawrence J., Jr., 215  
 Dorrenbos, David I., 328  
 Downing, Deborah J., 67  
 Drake, Lee B., 294  
 Duckworth, Michael, 330  
 Dungan, V. Craig, 328  
 Easterling, Randy, 67  
 Edwards, Joe D., 405  
 Ellison, Parker, 294  
 Evans, Jack, 253  
 Ervin, James W., Jr., 215  
 Fellows, William R., 68  
 Ferguson, Mitzi, 373  
 Fidei, Frank, 328  
 Field, Larry, 215, 253  
 Field, R. J., Jr., 169; 294  
 Ford, John Robert, 328  
 Frank-Tarsi, Mary Anne, 31  
 Freeland, Alan E., 171  
 French, Terry M., 405  
 Frye, Harry C., 28  
 Fulcher, Todd L., 68  
 Fullenwider, John P., 328  
 Furr, George, 28  
 Gaines, Kenneth, 434  
 Garretson, Roland, F., Jr., 294  
 Gearhart, Judith G., 28  
 Geissler, Walter R., 171  
 Gerald, Carolyn, 253

Gillespie, H. Lamar, 328  
 Glasgow, Richard W., 135  
 Gordan, Jim, 100  
 Hale, T. Eric, 28  
 Hall, Terrence, 68  
 Hamilton, George C., 30  
 Harman, Frank E., 405  
 Hatten, Karl, 369  
 Henderson, William, 253  
 Henson, L. C., 169  
 Hesdorffer, Eugene, 434  
 Hilbun, Benton, 171  
 Hill, J. Edward, 30, 434  
 Hillman, Joseph C., Jr., 294  
 Hodges, Rebecca, 30  
 Hopkins, L. G., 294  
 Hopper, William C., Jr., 215, 369  
 Hopson, W. Briggs, Jr., 215  
 Horowitz, Michael D., 100  
 Houston, Gerry Ann, 68  
 Howard, Martin L., Jr., 69  
 Hughes, Wayne, 67; 215, 328  
 Hull, Edgar W., 370  
 Ingram, Fred, 328  
 Jeffcoat, B. Thomas, 135  
 Jackson, Dan W., 253  
 Jackson, William G., 253  
 Johnson, Jeffrey A., 30  
 Johnson, Stephen P., 100; 294  
 Johnston, Walter E., 215  
 Jones, Scott, 253  
 Jordan, B. J., 328  
 Jordan, C. M., 328  
 Kanosky, Michael G., 328  
 Killelea, Donald, 328  
 King, Coleman, 434  
 Kitchenings, Ben, 434  
 Knight, Charles S., 373  
 Lake, Chester H., Jr., 253  
 Lambert, Stephen C., 68  
 Lay, Adron Keith, 370  
 Lee, J. Martin, 171  
 Lee, Zena Darcell, 434  
 Lippincott, Ken, 100  
 Lipscomb, Larry R., 370  
 Little, Nelson K., 370  
 Longest, Bruce, 215  
 Longest, John C., 328  
 Lowe, Terry, 328  
 Lubritz, Ronald R., 68  
 Lundy, McKinley S.,  
 Mallett, Robert A., 405  
 Mallett, Tara Scott, 30  
 Mann, Jr, John Evans, 30  
 Martin, Sherry A., 370  
 Martinolich, Andrew, 100  
 Massingill, S. Scott, 30  
 Mathis, Robert P., 171  
 May, Michael, 67; 215, 328  
 McBroom, Robert D., 215  
 McCraney, W. Thomas, Jr., 135  
 McDaniell, F. Ellen, 328  
 McDonnell, Fred J., 171  
 McKell, William M., Jr., 135  
 McKiever, Daniel J., 406  
 McLain, Patrick G., 370  
 McMillan, Beverly A., 136  
 McQueen, James N., 68



McVey, John H., Sr., 294  
 Meyers, William H., 135  
 Middleton, William A., 253, 434  
 Miller, Jimmy D., 328  
 Mills, Henry P., Jr., 406  
 Mills, Thomas P., 294  
 Mitchell, John R., 215  
 Molpus, William Mark, 294  
 Montalvo, Ray, Jr., 30  
 Montgomery, Tom, 253  
 Moore, Hugh C., 171  
 Moore, Paul, 295  
 Morgan, Frank J., Jr., 329  
 Morris, Glenn F., 68  
 Morrison, Francis, 136, 215, 253  
 Myers, Beverly, 294  
 Myers, Mitchell, J., 406  
 Newell, R. Bruce, 68  
 Norman, Carolyn R., 406  
 North, Darden H., 329  
 Ozborn, Charles A., 328  
 Parsons, Morris, 254  
 Partridge, R. Keith, 329, 434  
 Patel, Bharat R., 406  
 Patel, Harry R., 406  
 Patterson, W. J., 31  
 Payne, Hernando Cartes, 370  
 Peasley, Daniel J., 100, 434  
 Peeples, Sam, 254  
 Pennebaker, James B., 294  
 Polk, James D., 329  
 Powell, Rhonda Henderson, 295  
 Pulliam, Joe Stanley, 328  
 Puricelli, Mark S., 295  
 Reed, Alphonse M., 406  
 Reed, W. Ray, Jr., 295  
 Roberts, Donald L., 329  
 Roth, Stuart Todd, 329  
 Roy, Elizabeth N., 31  
 Ruvinsky, Marcelo, J., 215  
 Sandifer, Fred M., 68  
 Savoie, Buddy, 31, 68, 171, 215, 253, 329, 434  
 Schwartz, Robin H., 435  
 Scott-Conner, Carol, 68  
 Seicshnaydre, Michael A., 329  
 Segars, Kelly S., Sr., 31, 406  
 Senter, Jack, 370  
 Senter, Steve, 370  
 Sessums, Hildon, H., Jr., 217, 253  
 Shah, Nikhil, 329  
 Sharp, Richard, B., 330  
 Sharpton, Jr., Robert J., 31  
 Sheehan, Clyde A., 330  
 Shields, Rod A., 330  
 Short, Valerie A., 31  
 Skelton, Thomas N., 101  
 Slife, David M., 295  
 Smith, Glen, 293  
 Soucie, Pierre F., 31  
 Spell, B. G., 330  
 Spencer, William A., 135  
 Stanford, Keith, 31  
 Stone, Van D., III, 330  
 Sullivan, David W., 295  
 Sumrall, Doyle, 330  
 Sutherland, William K., 135  
 Tabb, W. Granville, Jr., 330

Taylor, Eugene E., 370  
 Taylor, Horton G., Jr., 370  
 Taylor, Max, 253  
 Terracina, Joseph R., 295  
 Terral, T. Gregory, 373  
 Thomas, Anthony L., 330  
 Thompson, Ed, 31  
 Thompson, James R., 136  
 Thigpen, J. Tate, 101  
 Tinsley, Plez, Jr., 217  
 Tumminello, Sam C., 330  
 Ugajin, Kazuo, 217  
 Vanderloo, Thomas E., 406  
 Vice, Guy T. Jr., 373  
 Waites, James C., 171, 373, 435  
 Walcot, D. Winn, 295  
 Walker, Billy, 69, 254  
 Walker, Jimmy, 254  
 Walker, Prentice, 373  
 Waller, Richard Edwin, 406  
 Walley, Schedell, 136  
 Walton, Benjamin F., 295  
 Walton, Bill, 217  
 Warden, Clark G., 373  
 Warrington, James E., 136  
 Washburn, Lisa K., 373  
 Weber, B. Michael, 330  
 Webster, Stevan A., 254  
 Wee, Abelardo S., 217  
 Wells, Peggy J., 254  
 Wells, Willie Lee, 373  
 Wender, David F., 373  
 Wesberry, Jess, Jr., 171  
 Wesson, Mathew B., 101  
 Wiggins, Chris E., 136  
 Wilcox, W. Paul, 406  
 Williams, David J., 67  
 Williams, Steven C., 69  
 Wilson, Jo P., 435  
 Whipple, Terry, 171  
 Whittington, Curtis D., Jr., 330  
 Whitty, Joseph Bingham, 435  
 Wong, Sidney, 217  
 Wooldridge, Tom, 217  
 Woody, Walter, 373  
 Wright, Timothy L., 373  
 Yelverton, Richard L., Jr., 295  
 Young, William D., 101

#### President's Page

a level playing field, [Mitchell] 192-PP  
 a tribute to Carl Evers, [Gates] 14-PP  
 carpe diem, [Mitchell] 422-PP  
 doctor, why do you make so much?, [Mitchell] 392-PP  
 gemutlichkeit, [Gates] 86-PP  
 reform, resolve, and reaffirmation, [Gates] 54-PP  
 reform revisited, [Gates] 120-PP  
 snowflakes, [Mitchell] 354-PP  
 the devil is in the details, [Mitchell] 238-PP  
 united voices, [Mitchell] 312-PP  
 why a tree falls, [Mitchell] 276-PP

#### R

##### Radiology

evaluation of mammographic stellate lesions, [Flowers and Powers] \*7

##### Rural Health Clinics

certified rural health clinics increase available health care, 352-S

#### S

##### Self-Treatment

common patient symptoms: patterns of self-treatment and prevention, [Habeeb and Gearhart] \*179

##### Sinus

functional endoscopic sinus surgery in children, [Haltom and Cannon] \*1  
 the bacteriology of chronic sinusitis in pediatrics, [Sturdivant and Cannon] \*183

##### Spondylosis

degenerative cervical disc disease, [McGuire]\*223

#### T

##### Testicular Vein

testicular vein and peripheral vein testosterone, follicle stimulating hormone, luteinizing hormone, and prolactin concentrations in a patient with androgen insensitivity syndrome, [Meeks, et al] \*263

#### U

##### UMC

Dr. Ball elected president of The American Aging Association, 25-N  
 Dr. Achord assumes helm of state ACP, 168-N  
 Dr. Halaris appointed Psychiatry Department Chairman, 62-N  
 Dr. Ho invited to serve on board of Scientific Counselors, 63-N  
 Dr. John H. Eichhorn receives Merck and Company Health Award, 249-N  
 Dr. Long receives Hofman Award, 421-N  
 Dr. Nelson to retire in 1994  
 Drs. Roberts and Morrison present results of study, 248-N  
 Dr. Robertson named director of continuing health professional education, 368-N  
 Greenwood resident named top graduate, 248-N  
 Kenneth St. John receives Scientific American Award, 25-N  
 Medical school building dedication honors first dean, 167-N  
 technology assists better view of inner space, 401-N  
 thanks, Dean Nelson, [Abraham] 423-E  
 the University of Mississippi Medical Center's Antenatal Diagnostic Unit: On the Cutting Edge of Tomorrow, [Roberts, et al] \*299  
 UMC Barnard Professors, 367-N  
 UMC receives \$6 million grant for cardiovascular study, 431-N  
**Utilization Review**  
 the law regarding utilization review, [Lockey] 277-E  
 the new PRO, [Cobb] 389-S

# AUTHOR INDEX

The letters used to explain in which department the matter indexed appears as follows: "A," Abstract; "C," Comment; "E," Editorial; "N," News; "L," Letters to the Editor; "PP," President's Page; "D," Delegates Report; "RS," Radiological Seminar; "ME," Medical Ethics; "BR," Book Review; "AP," Auxiliary Page; "S," Special Article; the asterisk (\*) indicates an original article in the Journal.

**A**  
Abraham, George, 87-E; 193-E; 313-E;  
423-E

**B**  
Bross, Michael H., \*42

**C**  
Cannon, C. Ron, \*1; \*183;  
Chauhan, Suneet P., \*35  
Cobb, Alton B., 240-L, 389-S  
Cohen, Theodore, 90-L  
Copland, D. Leigh, \*143  
Crane, Stephen M., \*143  
Currier, Robert D., 397-L

**D**  
Dabney, W. Moncure, 278-E  
Duddleston, David N., 233-S

**E**  
Edwards, Linda, 233-S  
England, Leslie E., 239-E; 355-E  
Evers, Jan, 91-L

**F**  
Feldberg, Murray, 425-C  
Field, Larry, \*147  
Files, Joe C., \*11; \*227; \*346  
Fisher, Luther C., \*147  
Flowers, W. Mel., Jr., \*7  
Furr, G. C., \*382

**G**  
Gates, William C., 14-PP; 54-PP; 86-PP;  
121-PP; 187-S  
Gearhart, Judith G., \*179

**H**  
Habeeb, George E. Jr., \*179  
Haltom, James R., \*1  
Hardy, James D., \*83  
Harper, Cecil, 411-S

**I**  
Iyer, Rathi V., \*107

**J**  
Johnston, Joseph E., 56-E; 155-E

**K**  
Kendig, Ronald J., \*147

**L**  
Lockey, Myron W., 15-E; 121-E; 278-E;  
393-E  
Lyles, R. Ray, 90-L

**M**  
Martin, James N., Jr., 299  
Martin, Rick W., 299  
McGuire, Robert A., \*223  
McIlwain, James S., Jr., 395-C  
Meeks, G. Rodney, \*143; \*263  
Megason, Gail C., \*107  
Mitchell, Don Q., 154-PP; 192-PP;  
238-PP; 277-PP; 312-PP; 354-PP;  
392-PP, 422-PP

Moore, James L., Jr., \*35  
Morgan, Frank J., \*46  
Morrison, John C., \*35; \*143, \*299

**N**  
Neral, Susan M., \*77

**P**  
Perry, Kenneth G., Jr., \*299  
Pittman, Kenneth P., \*143  
Polles, Alexis, \*77  
Powers, Cynthia I., \*7  
Pruett, Bruce, \*73, \*377

**R**  
Renfroe, Melanie S., \*263  
Replogle, William H., \*143  
Roberts, William E., \*299  
Roberts, William E., 411-S

**S**  
Saccoccia, Philip, Jr., 157-L  
Salvatore, Joseph R., 90-L  
Savoie, Felix H., III, \*259  
Smith, J. Clinton, \*107  
South, Dwalia, \*158; \*241; 315-C  
Stefani, Anne, \*42  
Sturdivant, Tara, \*183

**W**  
Weiner, William B., \*35  
Whitworth, Neil S., \*263

## TABLE OF PAGES

January .....	1 to 34	July .....	223 to 258
February .....	35 to 72	August .....	259 to 298
March .....	73 to 106	September .....	299 to 334
April .....	107 to 140	October .....	335 to 376
May .....	143 to 178	November .....	377 to 410
June .....	179 to 222	December .....	410 to 442



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## Index to Advertisers

Bristol-Myers Squibb Company -  
Pravachol ..... **third and fourth covers**

CompHealth ..... 435

Disability Determination ..... 441

Medical Assurance Co. of MS ..... **second cover**  
Medley and Company ..... 433  
MS Emergency Association ..... 441  
MS Physicians Insurance Company ..... 419  
MSMA Benefit Plan & Trust ..... 6

Premier Printing ..... 435

The Doctors' Company ..... 432  
Trustmark ..... 434

US Air Force Reserve ..... 429  
US Army Active ..... 424



## PRAVACHOL® (Pravastatin Sodium Tablets) CONTRAINDICATIONS

Hypersensitivity to any component of this medication.

Active liver disease or unexplained, persistent elevations in liver function tests (see WARNINGS).

**Pregnancy and lactation.** Atherosclerosis is a chronic process and discontinuation of lipid-lowering drugs during pregnancy should have little impact on the outcome of long-term therapy of primary hypercholesterolemia. Cholesterol and other products of cholesterol biosynthesis are essential components for fetal development (including synthesis of steroids and cell membranes). Since HMG-CoA reductase inhibitors decrease cholesterol synthesis and possibly the synthesis of other biologically active substances derived from cholesterol, they may cause fetal harm when administered to pregnant women. Therefore, HMG-CoA reductase inhibitors are contraindicated during pregnancy and in nursing mothers. **Pravastatin should be administered to women of childbearing age only when such patients are highly unlikely to conceive and have been informed of the potential hazards.** If the patient becomes pregnant while taking this class of drug, therapy should be discontinued and the patient apprised of the potential hazard to the fetus.

## WARNINGS

**Liver Enzymes:** HMG-CoA reductase inhibitors, like some other lipid-lowering therapies, have been associated with biochemical abnormalities of liver function. Increases of serum transaminase (ALT, AST) values to more than 3 times the upper limit of normal occurring on 2 or more (not necessarily sequential) occasions have been reported in 1.3% of patients treated with pravastatin in the U.S. over an average period of 18 months. These abnormalities were not associated with cholestasis and did not appear to be related to treatment duration. In those patients in whom these abnormalities were believed to be related to pravastatin and who were discontinued from therapy, the transaminase levels usually fell slowly to pretreatment levels. These biochemical findings are usually asymptomatic although worldwide experience indicates that anorexia, weakness, and/or abdominal pain may also be present in rare patients.

As with other lipid-lowering agents, liver function tests should be performed during therapy with pravastatin. Serum aminotransferases, including ALT (SGPT), should be monitored before treatment begins, every six weeks for the first three months, every eight weeks during the remainder of the first year, and periodically thereafter (e.g., at about six-month intervals). Special attention should be given to patients who develop increased transaminase levels. Liver function tests should be repeated to confirm an elevation and subsequently monitored at more frequent intervals. If increases in AST and ALT equal or exceed three times the upper limit of normal and persist, then therapy should be discontinued. Persistence of significant aminotransferase elevations following discontinuation of therapy may warrant consideration of liver biopsy.

Active liver disease or unexplained transaminase elevations are contraindications to the use of pravastatin (see CONTRAINDICATIONS). Caution should be exercised when pravastatin is administered to patients with a history of liver disease or heavy alcohol ingestion (see CLINICAL PHARMACOLOGY: Pharmacokinetics/Metabolism). Such patients should be closely monitored, started at the lower end of the recommended dosing range, and titrated to the desired therapeutic effect.

**Skeletal Muscle:** Rhabdomyolysis with renal dysfunction secondary to myoglobinuria has been reported with pravastatin and other drugs in this class. Uncomplicated myalgia has also been reported in pravastatin-treated patients (see ADVERSE REACTIONS). Myopathy, defined as muscle aching or muscle weakness in conjunction with increases in creatine phosphokinase (CPK) values to greater than 10 times the upper limit of normal was reported to be possibly due to pravastatin in only one patient in clinical trials (<0.1%). Myopathy should be considered in any patient with diffuse myalgias, muscle tenderness or weakness, and/or marked elevation of CPK. Patients should be advised to report promptly unexplained muscle pain, tenderness or weakness, particularly if accompanied by malaise or fever. **Pravastatin therapy should be discontinued if markedly elevated CPK levels occur or myopathy is diagnosed or suspected. Pravastatin therapy should also be temporarily withheld in any patient experiencing an acute or serious condition predisposing to the development of renal failure secondary to rhabdomyolysis, e.g., sepsis; hypotension; major surgery; trauma; severe metabolic, endocrine, or electrolyte disorders; or uncontrolled epilepsy.**

The risk of myopathy during treatment with lovastatin is increased if therapy with either cyclosporine, gemfibrozil, erythromycin, or niacin is administered concurrently. There is no experience with the use of pravastatin together with cyclosporine. Myopathy has not been observed in clinical trials involving small numbers of patients who were treated with pravastatin together with niacin. One trial of limited size involving combined therapy with pravastatin and gemfibrozil showed a trend toward more frequent CPK elevations and patient withdrawals due to musculoskeletal symptoms in the group receiving combined treatment as compared with the groups receiving placebo, gemfibrozil, or pravastatin monotherapy. Myopathy was not reported in this trial (see PRECAUTIONS: Drug Interactions). One patient developed myopathy when clofibrate was added to a previously well tolerated regimen of pravastatin; the myopathy resolved when clofibrate therapy was stopped and pravastatin treatment continued. **The use of fibrates alone may occasionally be associated with myopathy. The combined use of pravastatin and fibrates should generally be avoided.**

## PRECAUTIONS

**General:** Pravastatin may elevate creatine phosphokinase and transaminase levels (see ADVERSE REACTIONS). This should be considered in the differential diagnosis of chest pain in a patient on therapy with pravastatin.

**Homozygous Familial Hypercholesterolemia.** Pravastatin has not been evaluated in patients with rare homozygous familial hypercholesterolemia. In this group of patients, LDL is being reported that HMG-CoA reductase inhibitors are less effective because the patients lack functional LDL receptors.

**Renal Insufficiency:** A single 20 mg oral dose of pravastatin was administered to 24 patients with varying degrees of renal impairment (as determined by creatinine clearance). No effect was observed on the pharmacokinetics of pravastatin or its 3 $\alpha$ -hydroxy isomeric metabolite (SQ 31,906). A small increase was seen in mean AUC values and half-life (t<sub>1/2</sub>) for the inactive enzymatic ring hydroxylation metabolite (SQ 31,945). Given this small sample size, the dosage administered, and the degree of individual variability, patients with renal impairment who are receiving pravastatin should be closely monitored.

**Information for Patients:** Patients should be advised to report promptly unexplained muscle pain, tenderness or weakness, particularly if accompanied by malaise or fever.

**Drug Interactions:** Immunosuppressive Drugs, Gemfibrozil, Niacin (Nicotinic Acid), Erythromycin: See WARNINGS: Skeletal Muscle.

**Antipyrine:** Clearance by the cytochrome P450 system was unaltered by concomitant administration of pravastatin. Since pravastatin does not appear to induce hepatic drug-metabolizing enzymes, it is not expected that any significant interaction of pravastatin with other drugs (e.g., phenytoin, quinidine) metabolized by the cytochrome P450 system will occur.

**Cholestyramine/Colestipol:** Concomitant administration resulted in an approximately 40 to 50% decrease in the mean AUC of pravastatin. However, when pravastatin was administered 1 hour before or 4 hours after cholestyramine or 1 hour before colestipol and a standard meal, there was no clinically significant decrease in bioavailability or therapeutic effect. (See DOSAGE AND ADMINISTRATION: Concomitant Therapy).

**Warfarin:** In a study involving 10 healthy male subjects given pravastatin and warfarin concomitantly for 6 days, bioavailability parameters at steady state for pravastatin (parent compound) were not altered. Pravastatin did not alter the plasma protein-binding of warfarin. Concomitant dosing did increase the AUC and C<sub>max</sub> of warfarin but did not produce any changes in its anticoagulant action (i.e., no increase was seen in mean prothrombin time after 6 days of concomitant therapy). However, bleeding and extreme prolongation of prothrombin time has been reported with another drug in this class. Patients receiving warfarin-type anticoagulants should have their prothrombin times closely monitored when pravastatin is initiated or the dosage of pravastatin is changed.

**Cimetidine:** The AUC<sub>0-12h</sub> for pravastatin when given with cimetidine was not significantly different from the AUC for pravastatin when given alone. A significant difference was observed between the AUC's for pravastatin when given with cimetidine compared to when administered with antacid.

**Digoxin:** In a crossover trial involving 18 healthy male subjects given pravastatin and digoxin concurrently for 9 days, the bioavailability parameters of digoxin were not affected. The AUC of pravastatin tended to increase, but the overall bioavailability of pravastatin plus its metabolites SQ 31,906 and SQ 31,945 was not altered.

**Gemfibrozil:** In a crossover study in 20 healthy male volunteers given concomitant single doses of pravastatin and gemfibrozil, there was a significant decrease in urinary excretion and protein binding of pravastatin. In addition, there was a significant increase in AUC, C<sub>max</sub>, and T<sub>max</sub> for the pravastatin metabolite SQ 31,906. Combination therapy with pravastatin and gemfibrozil is generally not recommended.

In interaction studies with aspirin, antacids [1 hour prior to PRAVACHOL (pravastatin sodium)], cimetidine, nicotinic acid, or probucol, no statistically significant differences in bioavailability were seen when PRAVACHOL was administered.

**Other Drugs:** During clinical trials, no noticeable drug interactions were reported when PRAVACHOL was added to: diuretics, antihypertensives, digitalis, converting-enzyme inhibitors, calcium channel blockers, beta-blockers, or nitroglycerin.

**Endocrine Function:** HMG-CoA reductase inhibitors interfere with cholesterol synthesis and lower circulating cholesterol levels and, as such, might theoretically blunt adrenal or gonadal steroid hormone production. Results of clinical trials with pravastatin in males and post-menopausal females were inconsistent with regard to possible effects of the drug on basal steroid hormone levels. In a study of 21 males, the mean testosterone response to human chorionic gonadotropin was significantly reduced (p<0.004) after 16 weeks of treatment with 40 mg of pravastatin. However, the percentage of patients showing a  $\geq$ 50% rise in plasma testosterone after human chorionic gonadotropin stimulation did not change significantly after therapy in these patients. The effects of HMG-CoA reductase inhibitors on spermatogenesis and fertility have not been studied in adequate numbers of patients. The effects, if any, of pravastatin on the pituitary-gonadal axis in pre-menopausal females are unknown. Patients treated with pravastatin who display clinical evidence of endocrine dysfunction should be evaluated appropriately. Caution should also be exercised if an HMG-CoA reductase inhibitor or other agent used to lower cholesterol levels is administered to patients also receiving other drugs (e.g., ketoconazole, spiro lactone, cimetidine) that may diminish the levels or activity of steroid hormones.

**CNS Toxicity:** CNS vascular lesions, characterized by perivascular hemorrhage and edema and mononuclear cell

infiltration of perivascular spaces, were seen in dogs treated with pravastatin at a dose of 25 mg/kg/day, a dose that produced a plasma drug level about 50 times higher than the mean drug level in humans taking 40 mg/day. Similar CNS vascular lesions have been observed with several other drugs in this class.

A chemically similar drug in this class produced optic nerve degeneration (Wallerian degeneration of retinogeniculate fibers) in clinically normal dogs in a dose-dependent fashion starting at 60 mg/kg/day, a dose that produced mean plasma drug levels about 30 times higher than the mean drug level in humans taking the highest recommended dose (as measured by total enzyme inhibitory activity). This same drug also produced vestibulocochlear Wallerian-like degeneration and retinal ganglion cell chromatolysis in dogs treated for 14 weeks at 180 mg/kg/day, a dose which resulted in a mean plasma drug level similar to that seen with the 60 mg/kg dose.

**Carcinogenesis, Mutagenesis, Impairment of Fertility:** In a 2-year study in rats fed pravastatin at doses of 10, 30, or 100 mg/kg body weight, there was an increased incidence of hepatocellular carcinomas in males at the highest dose (p<0.01). Although rats were given up to 125 times the human dose (HD) on a mg/kg body weight basis, their serum drug levels were only 6 to 10 times higher than those measured in humans given 40 mg pravastatin as measured by AUC.

The oral administration of 10, 30, or 100 mg/kg (producing plasma drug levels approximately 0.5 to 5.0 times human drug levels at 40 mg) of pravastatin to mice for 22 months resulted in a statistically significant increase in the incidence of malignant lymphomas in treated females when all treatment groups were pooled and compared to controls (p<0.05). The incidence was not dose-related and male mice were not affected.

A chemically similar drug in this class was administered to mice for 72 weeks at 25, 100, and 400 mg/kg body weight, which resulted in mean serum drug levels approximately 3, 15, and 33 times higher than the mean human serum drug concentration (as total inhibitory activity) after a 40 mg oral dose. Liver carcinomas were significantly increased in high-dose females and mid- and high-dose males, with a maximum incidence of 90 percent in males. The incidence of adenomas of the liver was significantly increased in mid- and high-dose females. Drug treatment also significantly increased the incidence of lung adenomas in mid- and high-dose males and females. Adenomas of the eye Harderian gland (a gland of the eye of rodents) were significantly higher in high-dose mice than in controls.

No evidence of mutagenicity was observed *in vitro*, with or without rat liver metabolic activation, in the following studies: microbial mutagen tests, using mutant strains of *Salmonella typhimurium* or *Escherichia coli*; a forward mutation assay in L5178Y TK + / - mouse lymphoma cells; a chromosomal aberration test in hamster cells, and a gene conversion assay using *Saccharomyces cerevisiae*. In addition, there was no evidence of mutagenicity in either a dominant lethal test in mice or a micronucleus test in mice.

In a study in rats, with daily doses up to 500 mg/kg, pravastatin did not produce any adverse effects on fertility or general reproductive performance. However, in a study with another HMG-CoA reductase inhibitor, there was decreased fertility in male rats treated for 34 weeks at 25 mg/kg body weight, although this effect was not observed in a subsequent fertility study when this same dose was administered for 11 weeks (the entire cycle of spermatogenesis, including epididymal maturation). In rats treated with this same reductase inhibitor at 180 mg/kg/day, seminiferous tubule degeneration (necrosis and loss of spermatogenic epithelium) was observed. Although not seen with pravastatin, two similar drugs in this class caused drug-related testicular atrophy, decreased spermatogenesis, spermatocytic degeneration, and giant cell formation in dogs. The clinical significance of these findings is unclear.

**Pregnancy: Pregnancy Category X:** See CONTRAINDICATIONS.

Safety in pregnant women has not been established. Pravastatin was not teratogenic in rats at doses up to 1000 mg/kg/day or in rabbits at doses of up to 50 mg/kg/day. These doses resulted in 20x (rabbit) or 240x (rat) the human exposure based on surface area (mg/meter<sup>2</sup>). However, in studies with another HMG-CoA reductase inhibitor, skeletal malformations were observed in rats and mice. PRAVACHOL (pravastatin sodium) should be administered to women of child-bearing potential only when such patients are highly unlikely to conceive and have been informed of the potential hazards. If the woman becomes pregnant while taking PRAVACHOL, it should be discontinued and the patient advised again as to the potential hazards to the fetus.

**Nursing Mothers:** A small amount of pravastatin is excreted in human breast milk. Because of the potential for serious adverse reactions in nursing infants, women taking PRAVACHOL should not nurse (see CONTRAINDICATIONS).

**Pediatric Use:** Safety and effectiveness in individuals less than 18 years old have not been established. Hence, treatment in patients less than 18 years old is not recommended at this time. (See also PRECAUTIONS: General.)

## ADVERSE REACTIONS

Pravastatin is generally well tolerated, adverse reactions have usually been mild and transient. In 4-month long placebo-controlled trials, 1.7% of pravastatin-treated patients and 1.2% of placebo-treated patients were discontinued from treatment because of adverse experiences attributed to study drug therapy, this difference was not statistically significant. In long-term studies, the most common reasons for discontinuation were asymptomatic serum transaminase increases and mild, non-specific gastrointestinal complaints. During clinical trials the overall incidence of adverse events in the elderly was not different from the incidence observed in younger patients.

**Adverse Clinical Events:** All adverse clinical events (regardless of attribution) reported in more than 2% of pravastatin-treated patients in the placebo-controlled trials are identified in the table below, also shown are the percentages of patients in whom these medical events were believed to be related or possibly related to the drug:

Body System/Event	All Events %		Events Attributed to Study Drug %	
	Pravastatin (N = 900)	Placebo (N = 411)	Pravastatin (N = 900)	Placebo (N = 411)
Cardiovascular				
Cardiac Chest Pain	4.0	3.4	0.1	0.0
Dermatologic				
Rash	4.0	1.1	1.3	0.9
Gastrointestinal				
Nausea/Vomiting	7.3	7.1	2.9	3.4
Diarrhea	6.2	5.6	2.0	1.9
Abdominal Pain	5.4	6.9	2.0	3.9
Constipation	4.9	7.1	2.4	5.1
Flatulence	3.3	3.6	2.7	3.4
Heartburn	2.9	1.9	2.0	0.7
General				
Fatigue	3.3	3.4	1.9	1.0
Chest Pain	3.7	1.9	0.3	0.2
Influenza	2.4*	0.7	0.0	0.0
Musculoskeletal				
Localized Pain	10.0	9.0	1.4	1.5
Myalgia	2.7	1.0	0.6	0.0
Nervous System				
Headache	6.2	3.9	1.7*	0.2
Dizziness	3.3	3.2	1.0	0.5
Renal/Genitourinary				
Urinary Abnormality	2.4	2.9	0.7	1.2
Respiratory				
Common Cold	7.0	6.3	0.0	0.0
Rhinitis	4.0	4.1	0.1	0.0
Cough	2.6	1.7	0.1	0.0

\*Statistically significantly different from placebo.

The following effects have been reported with drugs in this class:

**Skeletal:** myopathy, rhabdomyolysis.

**Neurological:** dysfunction of certain cranial nerves (including alteration of taste, impairment of extra-ocular movement, facial paresis), tremor, vertigo, memory loss, paresthesia, peripheral neuropathy, peripheral nerve palsy.

**Hypersensitivity Reactions:** An apparent hypersensitivity syndrome has been reported rarely which has included one or more of the following features: anaphylaxis, angioedema, lupus erythematosus-like syndrome, polymyalgia rheumatica, vasculitis, purpura, thrombocytopenia, leukopenia, hemolytic anemia, positive ANA, ESR increase, arthritis, arthralgia, urticaria, asthena, photosensitivity, fever, chills, flushing, malaise, dyspnea, toxic epidermal necrolysis, erythema multiforme, including Stevens-Johnson syndrome.

**Gastrointestinal:** pancreatitis, hepatitis, including chronic active hepatitis, cholestatic jaundice, fatty change in liver, and, rarely, cirrhosis, fulminant hepatic necrosis, and hepatoma, anorexia, vomiting.

**Reproductive:** gynecomastia, loss of libido, erectile dysfunction.

**Eye:** progression of cataracts (lens opacities), ophthalmoplegia.

**Laboratory Test Abnormalities:** Increases in serum transaminase (ALT, AST) values and CPK have been observed (see WARNINGS).

Transient, asymptomatic eosinophilia has been reported. Eosinophil counts usually returned to normal despite continued therapy. Anemia, thrombocytopenia, and leukopenia have been reported with other HMG-CoA reductase inhibitors.

**Concomitant Therapy:** Pravastatin has been administered concurrently with cholestyramine, colestipol, nicotinic acid, probucol and gemfibrozil. Preliminary data suggest that the addition of either probucol or gemfibrozil to therapy with lovastatin or pravastatin is **not** associated with greater reduction in LDL-cholesterol than that achieved with lovastatin or pravastatin alone. No adverse reactions unique to the combination or in addition to those previously reported for each drug alone have been reported. Myopathy and rhabdomyolysis (with or without acute renal failure) have been reported when another HMG-CoA reductase inhibitor was used in combination with immunosuppressive drugs, gemfibrozil, erythromycin, or lipid-lowering doses of nicotinic acid. Concomitant therapy with HMG-CoA reductase inhibitors and these agents is generally not recommended (See WARNINGS: Skeletal Muscle and PRECAUTIONS: Drug Interactions).

## OVERDOSAGE

There have been no reports of overdoses with pravastatin.

Should an accidental overdose occur, treat symptomatically and institute supportive measures as required.



THE PRAVACHOL® DIRECTION  
IN LIPID MANAGEMENT

# Effective lipid management doesn't have to be tough



- Improves key lipids — significant reduction in LDL-C<sup>1</sup>
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**PRAVACHOL®**  
pravastatin sodium 20 mg tablets

PRAVACHOL is indicated as an adjunct to diet for the reduction of elevated total and LDL-cholesterol levels in patients with primary hypercholesterolemia (Types IIa and IIb) when the response to diet alone has not been adequate. Active liver disease or unexplained transaminase elevations, pregnancy and lactation are contraindications to the use of pravastatin sodium.

Please see CONTRAINDICATIONS, WARNINGS, PRECAUTIONS, and ADVERSE REACTIONS in the brief summary of prescribing information on the adjacent page.



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